Altered Dental Root Development in Long-Term Survivors of Pediatric Acute Lymphoblastic Leukemia

A Review of 17 Cases

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Seventeen patients treated for acute lymphoblastic leukemia by combination chemotherapy before their reaching 10 years of age were studied for altered dental root development of their premolar teeth. Five of the 17 patients showed subjective radiographic evidence of marked shortening of the premolar dental roots; 13 had thinning of the roots. A quantitative analysis was developed and verified, which disclosed a 63.33% to 84.38% reduction of premolar root length when compared with the mean of the historical controls. With recent significant increases in long-term survival rates of children with malignancies, altered dental development becomes an important factor to follow years after chemotherapy is discontinued. The findings of these chemotherapy-associated dental development changes impacts on the patient's quality of life and also can serve as a research tool to assess permanent effects of chemotherapy on normal tissue growth and development.

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CANCER AND ITS THERAPY causes profound systemic and oral effects. Acute oral effects secondary to administration of chemotherapy are well known.[1] Chronic oral effects have been seen and reported with radiation therapy,[2,3] but not conclusively with chemotherapy alone. This study determines the incidence and severity of altered dental root development in a group of long-term survivors of pediatric acute lymphoblastic leukemia (ALL) who were treated with chemotherapy before the age of 10 years.

With approximately 2500 children younger than 16 years afflicted with leukemia in the United States annually,[4] the exploration of the etiologic factors and prevalence of long-term sequelae is of importance to patients with leukemia and of interest to both the medical and dental communities.

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Before the development of the L-2 chemotherapy protocol in 1967, there were only two long-term survivors of childhood leukemia at Memorial Sloan-Kettering Cancer Center (MSKCC). The development of various chemotherapy protocols has greatly increased the long-term survival for this disease.[5] It is now possible to begin to detect some of the long-term side effects of treatment in these patients.

Review of the Literature

Chemotherapy alone has not previously been reported as producing aberration in skeletal development in humans. In a 1980 review article, Ziegler and Muggia did not report or cite definite evidence of long-term skeletal growth changes in humans attributed to chemotherapy alone.[6] A recent report[7] which reviewed dental anomalies in long-term survivors in childhood cancer included 23 patients who were treated with chemotherapy but without head and neck irradiation. Of these 23 patients, five were found to have tooth and root abnormalities. The authors believed that perhaps "other factors, *e.g.*, antibiotic medications, systemic disturbances, fever, and poor nutritional habits" might have been etiologic factors of the dental anomalies. Furthermore, that study did not detail the chemotherapy given or the specific diseases treated other than stating that the tumors were not primary to the oral region.

Arrested dental root development has been observed previously and attributed to various environmental and congenital etiologies. Known environmental causes are localized radiotherapy,[6–8] as well as trauma and iatrogenic orthodontic movement. Congenital conditions associated with arrested dental root development are dentinal dysplasia[9] and selected cases of dentinogenesis imperfecta[10] which have characteristic clinical and radiographic appearances. Thalassemia,[11] hypopituitarism,[12] hypoparathyroidism,[13] microcephaly[14] and Rothmund-Thompson syndrome[15] are associated with various systemic manifestations in addition to incomplete root development. Ando *et al.*[16] reported an association between racial variation and dental root length in maxillary incisor length of the Japanese population. The root length of third molars in a normal adult population is quite variable in general,[17] so that abnormal third molars do not weigh heavily.

In rats, studies have revealed that eruption and odontogenesis can be inhibited by antineoplastic agents. Mataki (1981) reported that colchicine and vinblastine produced dose-dependent inhibition of dentin formation in rat incisors.[18] An interruption of the continually growing incisor teeth of rats has been reported with triethanomelamine and particularly cyclophosphamide.[19–22] Alteration in odontogenesis in rat incisors, secondary to systemic cyclophosphamide administration, has been observed histologically in a number of studies.[23–25] Teratogenic effects have been found in rat fetuses when the pregnant rat was administered a single dose of various cancer chemotherapeutic agents.[26–38] In that series of experiments, the developmental anomalies were dependent on drug administration during the specific day of gestation, which provides experimental background consistant with the observations made in the currently studied patients.[39]

Methods and Materials

Study Population

All 17 of the patients studied were long-term survivors of childhood ALL treated with chemotherapy before the age of 10 years. In this study, the patients' dentitions were evaluated at age 14 years or older. The age for beginning chemotherapy ranged from 3.22 to 8.94 years (mean, 7 years 2 months).

The specific treatment modalities included six patients treated with the L-2 chemotherapy protocol (Fig. 1), nine patients were treated with the L-10 protocol (Figs. 2 and 3), and two patients received individualized chemotherapy (off-protocol). Only one of the off-protocol patients received cranial irradiation without inclusion of the dentition, whereas none of the L-2 or L-10 patients received cranial irradiation. All patients gave informed consent for the study, following a protocol reviewed and approved by the MSKCC Institutional Review Board.

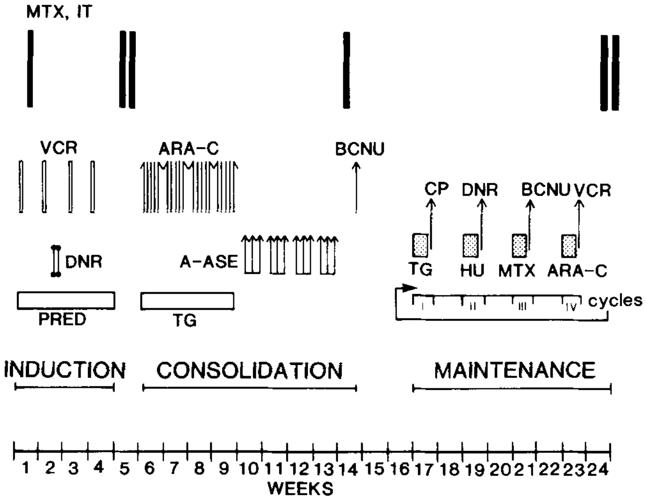

FIG. 1. Outline of the L-2 protocol. Induction: VCR (vincristine) 1.5 to 2 mg/m^2 IV: PRED (prednisone) 60 mg/m^2 orally: DNR (daunorubicin) 60 mg/m^2 IV. Consolidation: Ara-C (cytosine arabinoside) 150 mg/m^2 IV: TG (thioguanine) 75 mg/m^2 orally: A-ASE (L-Asparaginase) 60,000 IU/m^2 IV: BCNU (carmustine) 60 mg/m^2 IV. Maintenance: TG (thioguanine) 300 mg/m^2 orally: CP (cyclophosphamide) 600 mg/m^2 IV: HU (hydroxyurea) 2400 mg/m^2 orally: DNR (daunorubicin) 45 mg/m^2 IV: MTX (methotrexate) 10 mg/m^2 orally: BCNU (carmustine) 60 mg/m^2 IV: Ara-C (cytosine arabinoside) 150 mg/m^2 IV: VCR (vincristine) 2 mg/m^2 IV: MTX (methotrexate) 6.25 mg/m^2.

Dental Radiographic Study

A panoramic dental radiograph was obtained of all 17 patients studied. Periapical radiographs of the posterior

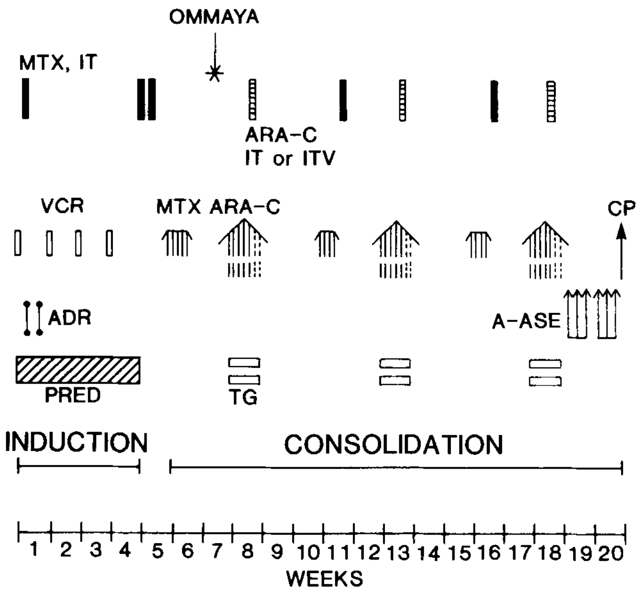

FIG. 2. Outline of the L-10 protocol, induction and consolidation. Induction: VCR (vincristine) 1.5 to 2 mg/m^2 IV. PRED (prednisone) 60 mg/m^2 orally: ADR (doxorubicin) 20 to 25 mg/m^2 IV. Consolidation: MTX (methotrexate) 15 mg/m^2 IV: Ara-C (cytosine arabinoside) 100 mg/m^2 IV every 12 hours: TG (thioguanine) 75 mg/m^2 orally every 12 hours: A-ASE (L-asparaginase) 60,000 IU/m^2 IV: CP (cyclophosphamide) 1200 mg/m^2 IV: MTX (methotrexate) 7 mg/m^2 IT or ITV: Ara-C (cytosine arabinoside) 25 mg/m^2 IT or ITV.

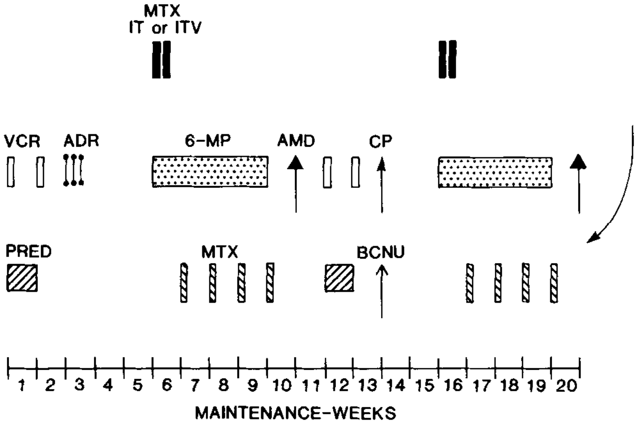

FIG. 3. Outline of the L-10 protocol, maintenance: VCR (vincristine) 1.5 to 2 mg/m^2 IV: PRED (prednisone) 180 mg/m^2 orally: 6-MP (mercaptopurine) 90 mg/m^2 orally: MTX (methotrexate) 20 mg/m^2 orally: AMD (dactinomycin) 750 mg/m^2 IV: CP (cyclophosphamide) 600 mg/m^2 IV: BCNU (carmustine) 60 mg/m^2 IV: MTX (methotrexate) 7 mg/m^2 IT or ITV.

teeth were obtained on which the two premolars and first molar were entirely within the same film. A long cone parallel technique was applied using a GE 700 unit.

Measurements

A Starrett dial caliper (L. S. Starrett, Athol, MA), accurate to 0.02 mm, was used to determine all of the radiographic tooth lengths. The premolar teeth were measured from the apex of the root to the corresponding buccal cusp tip. The maxillary first molars were measured from palatal root apex to mesial-buccal cusp tip, whereas the mandibular first molars were measured from mesial root apex to mesial-buccal cusp tip.

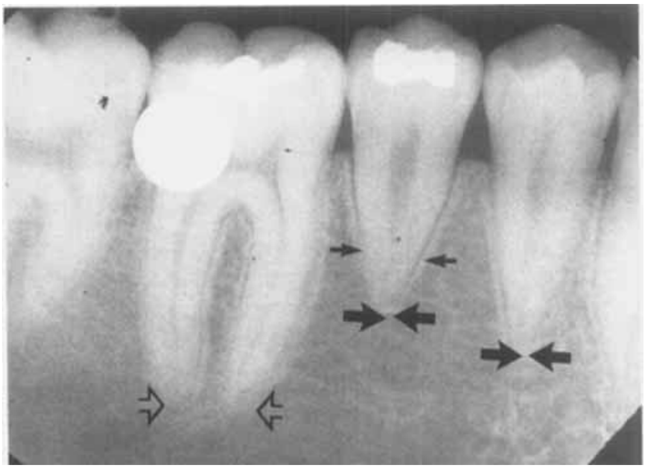

FIG. 4. Mandibular right side of a patient treated for ALL by the L-10 protocol from age 7 years 2 months showing moderate to severe shortening of the first and second premolars (large solid arrows) with slight to moderate tapering (small solid arrows) as compared to an essentially normal first molar with normally formed, full-length root apices (large open arrow). The white circle is an iron sphere measuring standard.

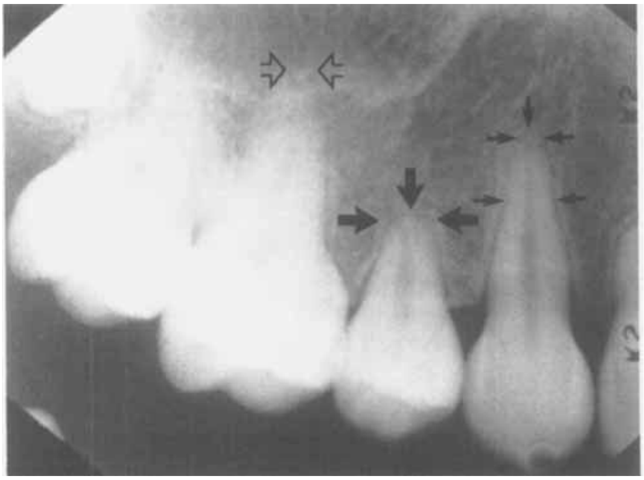

FIG. 5. Radiograph of the maxillary right side of a patient treated for ALL by the L-10 protocol from age 6 years 11 months showing bunting and severe shortening of the second premolar (large solid arrows) and moderate tapering and shortening (small solid arrows) of the canine. The first molar is essentially normal with the palatal root length shown by the large open arrows.

Subjective Assessment

A subjective assessment of the radiographs was done separately by two prosthodontists evaluating three parameters of root development: shortening of root length, morphologic blunting of the root apex, and root tapering/narrowing. Guidelines were established for subjective root "shortening." Premolar root lengths within a ± 2-mm range of the adjacent first molar root length were considered "within normal limits." A premolar root which appeared up to one third shorter was graded as "mild" shortening. A greater than one third loss of root length was graded as "severe" shortening (Fig. 4).

"Blunting" of the root apex refers to an apex that develops in a stunted manner as opposed to a characteristic narrower convex outline (Fig. 5).

"Tapering" or narrowing of the root was classified as "mild" if the root apex ended in a sharp thin point restricted to the apical-third of the root and "severe" if more than the apical-third of the root morphology was thinned and constricted (Fig. 6).

Quantitative Assessment

Ratio of radiographic length technique: A controlled radiographic technique that minimized distortion and a statistically verified analysis technique were developed and employed with this study. The technique employs a radioopaque metal sphere, placed buccal to the teeth just before taking the parallel technique radiograph, to enable measurement of horizontal and vertical length distortion and the use of the premolar-to-molar tooth length ratios, to correct for lengthen distortions of the tooth image on the x-ray film. The rationale for the methods and procedures requires some explanation for those unfamiliar with intraoral dental radiography. In a typical dental radiograph, the measured lengths of a patient's teeth on an x-ray film can be quite different from the actual lengths owing to angular and magnification distortions.[40–43] Such distortions made it difficult initially to quantitatively assess altered dental root development in long-term survivors of pediatric leukemia without specific corrections. The current study attempts to address this problem by focussing on relative dental deformation instead of actual deformation.

Specifically, this study examines the ratio of the measured radiographic length of each premolar to that of its adjacent first molar. These ratios were considered because it was empirically observed that there is relatively little alteration in the first molar morphology within this population. Therefore, by expressing the length of each premolar as a fraction of the first molar, the distortion problem mentioned above can be avoided.

For ease of exposition, the following notations are introduced: P1 = length of the first premolar as measured on the radiograph; P2 = length of the second premolar as measured on the radiograph; M1 = length of the first molar as measured on the radiograph;

$$P1{:}M1 = \frac{P1}{M1};\ \text{and}\ P2{:}M1 = \frac{P2}{M1}.$$

The validity of the ratio approach in assessing alteration in dental root development is best explained by Figure 7 where it is assumed that the distance from the first or second premolar to the first molar is negligibly small relative to the distance from the x-ray source to the teeth. From elementary geometry,

$$\frac{BC}{AC} = \frac{EF}{DF}$$

Hence, any alteration of the first (or second) premolar relative to the basically unaffected first molar, namely the ratio BC to AC, both of which are unknown, is simply given by the ratio of EF to DF, both of which are directly measurable from the x-ray film.

Historical control selection: Exploratory data analytic techniques were used in the selection of ten historical control studies that were collected and reviewed by Verhoeven *et al.*[44] to ensure that these constitute a representative sample comparable to the patient study population.

An observed ratio below the usual $100(1 - \alpha)\%$ confidence interval of the historical mean is to be regarded as a definite reduction. The confidence interval is given by

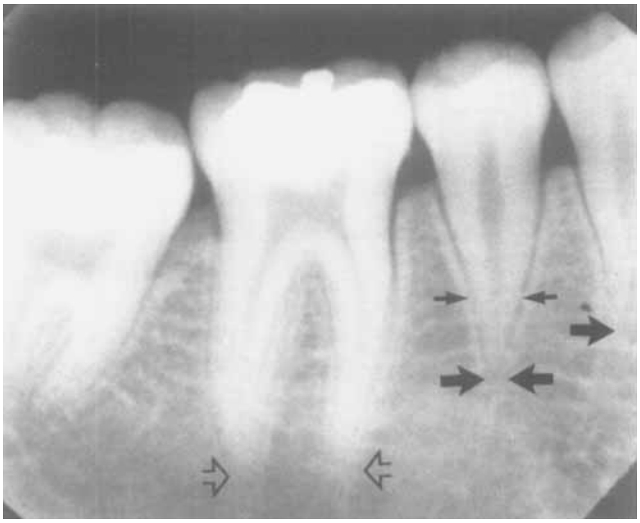

FIG. 6. Radiograph of mandibular right side of a patient treated for ALL by the L-10 protocol from age 8 years 0 months showing severe tapering (small solid arrows) and moderate shortening (large solid arrows) of the first and second premolars. The first molar is essentially normal with the root apices shown by large open arrows.

$$\bar{X} \pm t(1 - \frac{\alpha}{2}; N - 1)\frac{S}{\sqrt{N}}$$

where $\bar{X}$ is the sample mean and S is the sample standard deviation of the ratio based on a sample of size N, and $t(1 - \frac{\alpha}{2}; N - 1)$ is the upper $\frac{\alpha}{2}$ percentage cutoff point of the Student's *t* distribution with N − 1 degrees of freedom.

For the patients we studied, P1, P2, and M1 represent potentially distorted lengths measured on a radiograph of individual *in vivo* teeth, whereas for the historical controls,

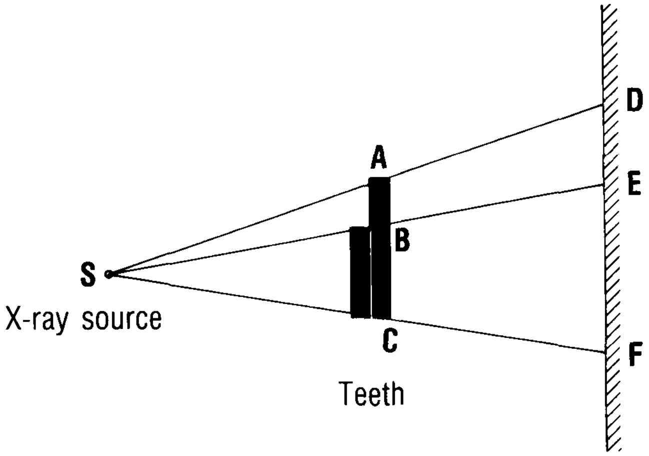

FIG. 7. Diagramatic representation of two adjacent teeth of lengths AC and BC and their radiographic projection to an intra-oral x-ray film. Although radiographic lengths (DF and EF) are longer than normal, they are in the proportion BC:AC = EF:DF.

TABLE 1. Tooth Length Averages of Historical Studies*

Study	LM1	LP1	LP2	UM1	UP1	UP2
Aprile	21.0	22.4	23.0	22.0	21.0	21.5
Bjorndal	22.0	22.9	22.3	22.3	22.3	22.3
Bouland	21.0	22.0	23.0	22.0	21.0	22.0
Dieulafe	21.0	21.6	22.3	20.8	20.6	21.5
Marseillier	21.0	23.0	23.5	22.3	21.0	21.0
Morike	21.0	21.6	23.2	21.3	21.7	21.5
Muhlreiter	22.8	22.8	23.2	21.3	21.7	21.5
Pucci	21.9	21.9	22.3	21.3	21.5	21.6
Sauvez	20.9	21.8	22.3	20.7	20.7	21.5
Wheeler	21.5	22.5	22.5	20.0	22.5	22.5
Mean	21.41	22.25	22.76	21.40	21.40	21.69
Median	21.00	22.20	22.75	21.30	21.25	21.50
Standard deviation	0.64	0.54	0.47	0.76	0.65	0.45
Maximum	22.80	23.00	23.50	22.30	22.50	22.50
Minimum	20.90	21.60	22.30	20.00	20.60	21.00

* Historical studies selected from those reviewed by Verhoeven *et al.*[40]

these quantities were usually averages of anatomic lengths for a series of extracted teeth which included some small mechanical measurement error.

Results

On subjective assessment, five of the 17 patients had very marked shortening of the premolar dental roots. Thirteen of the patients had thinning of the apical portion of selected molar, premolar, and/or canine teeth. The quantitative assessment required the establishment of a "control" standard of tooth length and the refinement of the radiographic technique to allow valid comparison of the subjects tooth length.

TABLE 2. Tooth Length Ratios for Historical Studies*

Study	L P1:M1	L P2:M1	U P1:M1	U P2:M1
Aprile	1.0667	1.0952	0.9546	0.9773
Bjorndal	1.0409	1.0136	1.0000	1.0000
Bouland	1.0476	1.0952	0.9546	1.0000
Dieulafe	1.0286	1.0619	0.9904	1.0337
Marseillier	1.0952	1.1191	0.9417	0.9417
Morike	1.0286	1.1048	1.0188	1.0094
Muhlreiter	1.0000	1.0175	1.0188	1.0094
Pucci	1.0000	1.0183	1.0094	1.0141
Sauvez	1.0431	1.0670	1.0000	1.0387
Wheeler	1.0465	1.0465	1.1250	1.1250
Mean	1.0397	1.0639	1.0013	1.0149
Median	1.0420	1.0644	1.0000	1.0094
Standard deviation	0.0285	0.0391	0.0517	0.0475
Maximum	1.0952	1.1190	1.1250	1.1250
Minimum	1.0000	1.0136	0.9417	0.9417

* Historical studies selected from those reviewed by Verhoeven *et al.*[40]

Table 1 gives the reported lengths of the extracted first molars, first premolars, and second premolars of the historical control studies. The letters L and U differentiate the mandibular (lower jaw) from the maxillary (upper jaw). The corresponding ratios for the historical control were calculated (Table 2). Statistical analysis of the normal probability plots (not shown here) indicated that the distribution of each of the four ratios had slightly longer tails than that of a "normal" variable. With only a small sample of historical controls, however, it was deemed more practical to perform statistical analysis on the ratios under standard normal assumption rather than to employ a more complicated statistical procedure.

For the historical controls, $N = 10$ and was α assigned the value 0.05 so that the 95% confidence interval was obtained. With $t(0.975; 9) = 2.2620$, the confidence intervals were calculated as follows:

$$LP1{:}M1 = (1.0193, 1.0601)$$

$$LP2{:}M1 = (1.0359, 1.0920)$$

$$UP1{:}M1 = (0.9644, 1.0382)$$

$$UP2{:}M1 = (0.9810, 1.0488)$$

Tables 3 and 4 summarize the tooth length ratios, chemotherapy protocols and the age at diagnosis of 17 pediatric leukemia patients. The additional letters L and R refer to the left and right sides, respectively (thus for example, LR P1:M1 stands for the ratio of the length of the mandibular [lower] right first premolar to that of the mandibular right first molar). The symbol * represents a missing value due to prior extraction of the tooth. The ratios are plotted with reference to the 95% confidence interval (Fig. 8) of the historical mean.

Paired sample *t* tests for any left–right difference yielded the following *P* values:

$$LLP1{:}M1 \textit{ versus } LRP1{:}M1 = 0.32$$

$$LLP2{:}M1 \textit{ versus } LRP2{:}M1 = 0.57$$

$$ULP1{:}M1 \textit{ versus } URP1{:}M1 = 0.14$$

$$ULP2{:}M1 \textit{ versus } URP2{:}M1 = 0.18$$

The data seemed to suggest that there is more agreement between the left and right ratios in the mandibular than in the maxillary. For the latter, the right premolars appeared to be more affected than the left premolars. All the test results, however, were not significant even at the 0.10 level. Therefore, it may be concluded that there is no real difference between the left and right ratios.

The mandibular and maxillary ratios were compared to the confidence intervals established earlier for the historical control studies (Fig. 7). For the mandibular teeth,

TABLE 3. Mandible Tooth Length Ratios

Patient	Protocol	Age at diagnosis	LL P1:M1	LL P2:M1	LR P1:M1	LR P2:M1
1	L-10	7.02	*	0.8551	0.9352	0.8430
2	L-2	6.05	1.0663	*	1.0580	*
3	Individual	2.28	1.1518	1.0095	1.1608	1.0385
4	L-10	4.90	*	1.0118	1.0140	1.0248
5	L-2	5.16	1.0563	1.0732	1.0028	1.0552
6	L-10	8.90	0.9995	1.0128	0.9427	0.9923
7	L-10	8.01	0.9230	0.8527	0.7732	0.8441
8	L-10	6.92	*	0.7556	*	0.7974
9	L-10	5.04	0.9367	0.8953	1.0177	0.9833
10	L-2	6.20	0.9635	1.1019	0.9756	1.0632
11	L-2	8.94	1.0153	1.0771	1.0193	1.0485
12	L-10	8.21	1.0331	0.9743	1.0234	0.9915
13	Individual	7.88	0.9585	0.6712	0.9527	0.6518
14	L-10	7.22	0.9285	0.8482	0.8894	0.8273
15	L-10	3.22	1.1998	1.0103	1.1816	0.9828
16	L-2	8.21	0.9275	0.9136	0.9591	0.9971
17	L-2	4.13	1.0192	1.0364	1.0205	1.0478

* Missing tooth.

23 of 32 P2:M1 ratios (71.88%) were below the confidence interval. However only 19 of 30 P1:M1 ratios (63.33%) were below the confidence interval. For the maxillary teeth, there was more pronounced deformation: 21/29 (72.41%) in the case of P1:M1, and 27/32 (84.38%) in the case of P2:M1.

Discussion

Based on the evidence of these 17 long-term survivors of ALL studied to date, there appears to be a selected incidence of altered dental root development in a number of patients. Twelve of the patients were found to have thinning of the apical portion of selected molar, premolars, and/or canine teeth on subjective assessment.

A statistically significant percentage of premolars in these patients were shorter than the historical mean. The most affected tooth appeared to be the maxillary second premolars.

Age at the time of treatment appears to have a degree of influence on the length of selected teeth. The mandibular first premolars appeared shorter in relation to the length of their corresponding first molars as the age of the patient increased at time of treatment. The linear negative correlation of age with the mandibular P1:M1 ratio might be explained by (1) a length increase of M1 with age,

TABLE 4. Maxillary Tooth Length Ratios

Patient	Protocol	Age at diagnosis	UL P1:M1	UL P2:M1	UR P1:M1	UR P2:M1
1	L-10	7.02	0.7522	0.7194	0.7417	0.6873
2	L-2	6.05	0.9685	*	0.9367	*
3	Individual	2.28	0.9853	0.8481	0.9011	0.8153
4	L-10	4.90	0.9546	0.9641	0.9100	0.9173
5	L-2	5.16	0.9060	0.9076	0.9016	0.8651
6	L-10	8.90	0.8888	0.8406	0.9093	0.8771
7	L-10	8.01	0.7823	0.8057	0.8022	0.7531
8	L-10	6.92	*	0.6369	*	0.6670
9	L-10	5.04	0.8494	0.9023	*	0.8792
10	L-2	6.20	0.9755	1.0064	0.9892	1.0165
11	L-2	8.94	0.8914	0.8967	*	0.9894
12	L-10	8.21	0.9983	0.9578	0.8890	0.8890
13	Individual	7.88	0.6600	0.6762	0.5109	0.5860
14	L-10	7.22	0.8330	0.6996	0.8692	0.7514
15	L-10	3.22	1.0657	1.0698	*	0.8793
16	L-2	8.21	0.9032	0.9087	0.9859	0.9686
17	L-2	4.13	1.0101	1.0058	0.8508	0.8946

* Missing tooth.

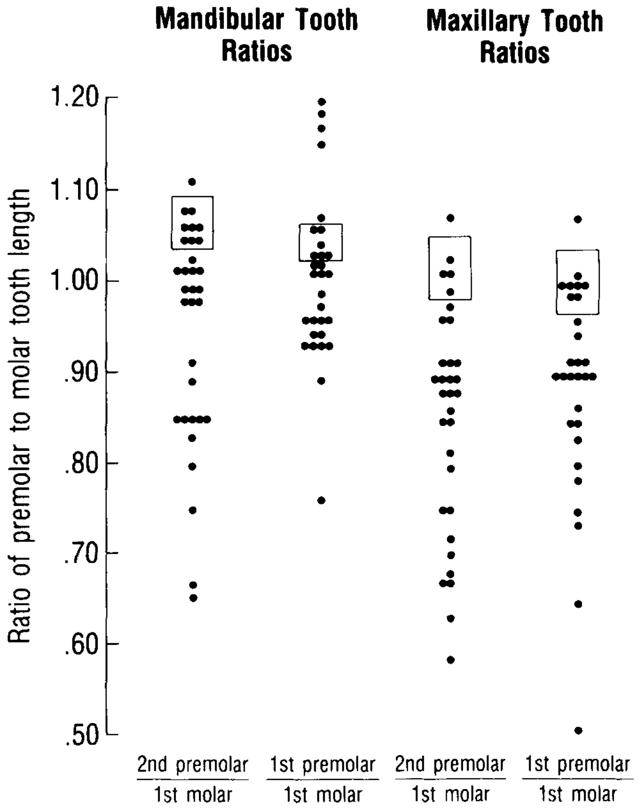

FIG. 8. Graph showing the premolars to molar tooth length ratios. The rectangles depict the 95% confidence interval of the historical mean of premolar to molar tooth ratios. Notice the large number of values below normal mean particularly those below 0.80 indicated significant clinical shortening.

indicating that M1 was effected in the younger population; (2) an effect and resultant shortening of P1 in older patients of this population with M1 remaining constant; or (3) a combination of the above two phenomena. Generally, the first molars develop their dental root structure three to four years before their corresponding premolars.[45] The longitudinal development of the first molar roots is generally complete by the age of 8 years. The premolar root structures generally are not complete until the age of 13 years. Therefore, altered dental root development may likely take place in children treated with chemotherapy just up to the teens.

Alteration of dental root form did not appear to be associated with the sex of the patient. The L-10 protocol may have an increased tendency toward more pronounced root shortening than the L-2 patients. Statistically, there was a greater tendency for L-10 patients to have shortened roots, particularly the second premolars. As additional patients are evaluated, varied effects of different chemotherapy protocols may become apparent. As more and more children survive ALL and other childhood malignancies to adulthood, continued efforts to study these increasing numbers of patients are being made. This will allow more definitive answers to the severity and incidence of long-term chemotherapy side effects on dental root development as well as the effect of age of treatment on development.

Significance

This is the first study to systematically study and identify altered dental root development associated with chemotherapy only. All previous studies found root alterations associated with radiation therapy which included the jaws. The potential causes include direct inhibiting effects of chemotherapy, altered marrow milieu associated with the presence of leukemic cells in the jaws, or systemic factors that alter growth, such as severity of leukemia at initial presentation, generalized growth suppression, hormone suppression, intensity of chemotherapy induction, *etc.* Research continues to investigate the causes of the alterations noted.

Fifty percent long-term survival currently is projected for the 5000 children younger than 16 years who develop cancer annually, and for virtually all of them chemotherapy will be a significant part of the treatment. With regard to child seen who received chemotherapy only (without cranial irradiation) for ALL between the ages of 4 to 10 years, this study demonstrated dental root developmental anomalies subjectively in 76.5% of the patients and quantitatively in 63.3% to 84.4% of their premolar teeth. Therefore, at least one complex organ system (the dentition) underwent significant alteration of development. Previously, with few survivors of pediatric cancer, the primary goal was increasing the percent and duration of remission. With increased survival, a new discipline of medicine must emerge that addresses studying and treating the effects of the life saving therapy. The findings of this study have significance to (1) the "cured" patient who is currently off of treatment; (2) current and future pediatric cancer patients who require chemotherapy; and (3) oncologists who treat and/or research malignancies which are treated with chemotherapy.

The cured patient who received chemotherapy before age 10 years should receive a single, careful periapical dental radiographic survey to determine the presence and degree of dental root alteration. This survey should be conducted before the extraction of any permanent teeth (especially if orthodontics is to be performed) or in the latter teens (15–19 years) for the asymptomatic patient. Patients should be advised of the findings and a preventive program of dental care should be emphasized that would delay the early loss of compromised teeth due to periodontal disease. The loss of supporting bone in normal patients due to periodontal disease accounts for the majority of tooth loss in people older than 30 years. Patients with shorter roots can be expected to loose the teeth earlier than if the roots were normal. The periodontal preventive care recommended involves meticulous oral hygiene and more frequent dental visits to evaluate and maintain periodontal health.

For patients who require orthodontics, the treatment plan may have to be altered due to the root shortening. The first premolar teeth often are extracted as part of orthodontic therapy for severe crowding or jaw protrusion. There also is the possibility of causing excessive root resorption, if the forces of tooth movement are not physiologic. Thus, if the first premolars have better root structure than the second premolars, then the weaker second premolar teeth should be extracted and the orthodontic therapy modified for gentler forces. The risk of not identifying possibly more rapid root resorption from orthodontic therapy must be weighed against the risks of more frequent dental radiographs.

Medical ethics of informed consent may require disclosing altered dental root development as a possible, albeit minor, consequence of the chemotherapy planned. As research proceeds into the mechanism of chemotherapeutically-induced dental alteration, changes in protocols will have to be tested for changes in root alterations.

Conclusions

Seventeen long-term survivors of childhood leukemia treated with chemotherapy before the age of 10 years were evaluated regarding their dental root development. Only one of the patients received cranial irradiation in addition to chemotherapy. The dentitions were evaluated with panoramic and periapical radiographs at age 14 years or older.

On subjective assessment, five of the 17 patients had very marked shortening of the premolar dental roots. Thirteen of the patients had thinning of the apical portion of selected molar, premolar, and/or canine teeth. Quantitatively, a comparison of the ratios of the first and second premolars as compared to their corresponding first molars revealed significant deviation from previous control studies. The least affected were the mandibular P1:M1 ratios, with 63.33% below the confidence interval, whereas the most affected were the maxillary P2:M1 ratios, with 84.38% below the confidence interval. Therefore, a significant number of patients were found to have dental anomalies associated with their therapies.

Root tapering occurred equally in both L-2 and L-10 patients. Root shortening occurred more frequently plus more markedly in the L-10 patients studied, than the L-2 patients. Age of treatment also may be a factor in regard to incidence of dental anomalies, because the premolars undergo their most significant root development when the majority of these patients are treated.

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