

## The spectrum of dental manifestations in vitamin D-resistant rickets: implications for management

W. Kim Seow, BDS, MDS, FRACDS S.C. Latham, MBBS, FRACP

### Abstract

*Vitamin D-resistant rickets (VDRR), usually inherited in an X-linked dominant manner, is the most common type of rickets in developed countries today. This analysis of 13 patients affected by the disease indicates that dental manifestations occur in a wide spectrum of severity which is determined by several factors including heredity, sex, and medical treatment. The spectrum of severity of dental manifestations can be classified into Grades I-III in order of increasing severity. Grade I severity includes near normal dentition while Grade II indicates involvement of only a few teeth. Grade III includes greatly enlarged pulp chambers, multiple dental abscesses, and poorly calcified dentin. Strategies for the prevention of dental abscesses in each grade of severity should be used appropriately.*

The most common form of rickets in developed countries today is an inherited form of rickets known as vitamin D-resistant rickets (VDRR).<sup>1</sup> This condition, first described by Albright et al.,<sup>2</sup> also is known by various other names such as familial hypophosphatemia, vitamin D-refractory rickets, and phosphate diabetes. The disease usually is inherited in an X-linked dominant manner,<sup>3</sup> with an affected male passing the defective gene to all his daughters and none of his sons. In contrast, an affected female will pass the gene to half of the daughters and half of the sons.

The pathogenesis of VDRR results from a selective disorder of transepithelial transport of phosphate in the kidney, leading to decreased tubular reabsorption of phosphate and persistent hypophosphatemia.<sup>4</sup> The low levels of serum phosphate lead to defective calcification, with signs and symptoms of rickets often appearing at about 8-10 months of age. These signs include lateral bowing of the legs, frontal bossing, enlargement of the costochondral junctions, scoliosis, and lordosis. Medical management of

VDRR consists of phosphate replacement together with vitamin D given usually in the form of calcitriol.

The dental manifestations of VDRR are quite characteristic, with multiple "spontaneous" dental abscesses being reported most often.<sup>5-15</sup> These abscesses result from pulp exposures which occur easily due to the large pulp chambers usually evident in the dental radiographs of these patients. Histological studies often show abnormal dentin calcification with large calcospherities and tubular defects extending close to the dentino-enamel junction.<sup>5-8</sup>

Although previous studies on patients with VDRR have described the above dental manifestations, little emphasis has been placed on the prevention of dental abscesses. In addition, although it has been reported that hypophosphatemia occurs in varying degrees of severity, it is not known whether dental manifestations are affected accordingly.

The authors studied several patients from different families with confirmed diagnoses of VDRR to determine the spectrum of dental manifestations of the disease and the factors associated with these variations. The objective of the study was to provide guidelines in the prevention of dental abscesses which may be a constant problem in affected patients.

### Spectrum of Dental Manifestations

Thirteen patients from 6 different families were studied. A summary of the characteristics of these patients are shown in Table 1. Based on dental manifestations and the need for treatment and prevention of dental abscesses, the patients can be divided into 3 main grades as follows.

Grade I is comprised of patients who show minimal or no dental manifestations of VDRR. These patients require only routine dental care and preven-

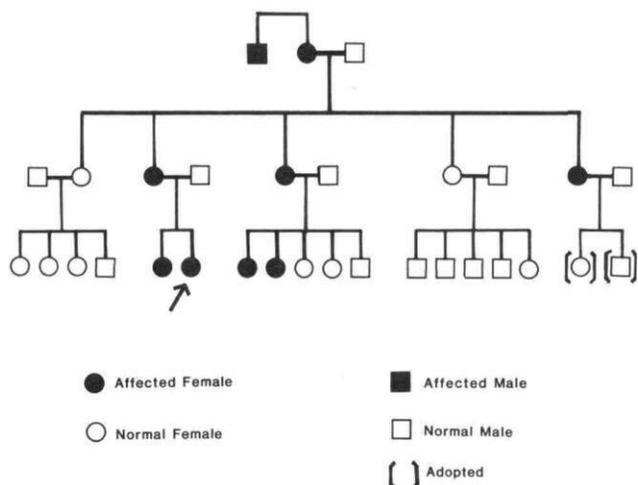


FIG 1. Family pedigree of a female (Case 12) affected by VDRR, showing typical transmission of the disease in an X-linked dominant manner. Arrow shows proband.

tive measures. Seven patients in the series can be categorized into this group (Cases 6–13).

Grade II patients are those who show moderate dental manifestations of the disease, only a few teeth are involved, and the prophylactic procedures required are moderate. Four patients in the series can be placed into this group (Cases 3–5).

Grade III is comprised of patients who show severe dental manifestations of the disease and require extensive treatment and aggressive prophylactic measures to prevent the development of dental abscesses. Two patients in the series can be placed into this group (Cases 1 and 2).

Representative cases of each of the above classes are discussed.

## Illustrative Cases

### Grade I (Case 12)

This female patient was 13 years old upon referral to the University Dental School. She was about 9 months old when VDRR was diagnosed and treatment with phosphate and calcitriol started. She inherited the disease from her mother (Case 11). An older sibling (Case 13) also was affected. The family pedigree chart shown in Fig 1 reveals typical transmission of the disease in an X-linked dominant manner.

At the time of dental examination, apart from a short stature (height 130.5 cm, 3<sup>rd</sup> percentile) and slight bowing of the legs, she showed minimal skeletal signs of rickets. Clinical examination revealed all permanent teeth except third molars were erupted. No caries or periodontal abnormalities were detected, but the maxillary right permanent molar showed enamel hypoplasia. No dental abscesses were noted and there was no history of any abscesses in

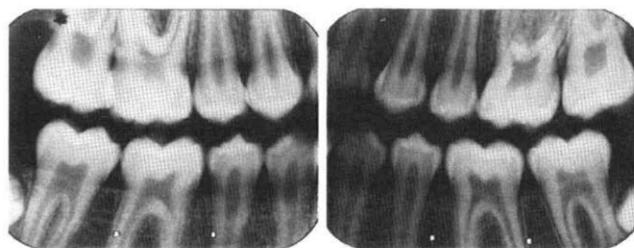


FIG 2. Bite-wing radiographs of a female (Case 12) affected by VDRR. The dental manifestations are of Grade I severity with near normal calcification of the teeth. Note normal sizes of the pulp chambers.

the primary dentition. Radiographic examination revealed normal calcification of enamel and dentine with the pulp chambers fairly normal in appearance (Fig 2). As the teeth were essentially normal, no prophylactic measures for dental abscesses were required. However, fissure sealants were placed on posterior teeth as routine preventive procedures for dental caries.

The patient's sibling (Case 13) showed essentially similar clinical and radiographic features, with minimal dental signs of VDRR. Of interest, too, is the fact that the mother (Case 11) also exhibited minimal signs of the condition and had no history of dental abscesses despite moderate skeletal manifestations of the disease.

### Grade II (Case 5)

This female patient was referred to the Dental School at age 13 years. She was diagnosed as having VDRR at the age of 18 months and had been on phosphate and calcitriol therapy continually. She inherited the disease from her mother (Case 10). Her brother, the only sibling, was unaffected. The mother, who was the first-known member of the family with the condition, was diagnosed herself only a few years previously. At the time of dental examination skeletal manifestations of rickets were obvious—bowing of the legs, frontal bossing, and short stature (height 124.8 cm, < 3<sup>rd</sup> percentile).

At the time of dental examination, all her perma-

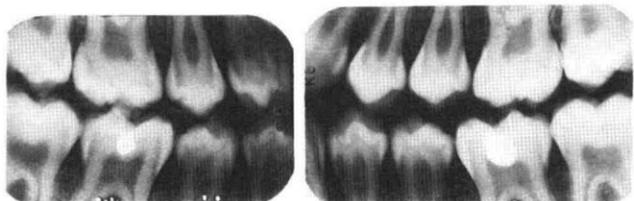


FIG 3. Bite-wing radiographs of a female (Case 5) with VDRR. The dental manifestations are of Grade II severity with moderate enlargement of the pulp chambers.

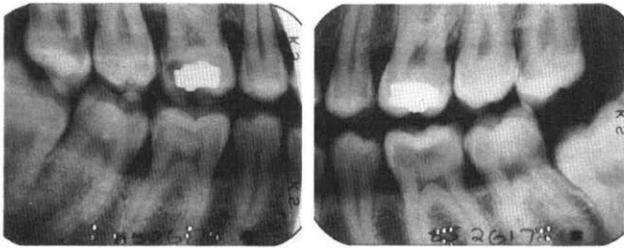


FIG 4. Bite-wing radiographs of affected mother of Case 5 taken at initial examination. Although she has VDRR, the dental manifestations are minimal. The pulp chambers of the teeth appear normal and no abscesses have developed.

dent teeth except the maxillary canines and third molars were erupted. Apart from hypoplasia of the maxillary right central incisor, no abnormalities were detected intraorally. Radiographic examination of the teeth revealed enlarged pulp chambers of all permanent teeth (Fig 3).

Clinical history confirms that Case 5 was affected to a lesser degree than Case 1. Although there was a history of 3 "spontaneous" dental abscesses of the primary teeth at the age of 8-9 years, the patient had not experienced an abscess of the permanent teeth by 13 years.

Although this patient was less severely affected compared to Case 1, she still required prophylactic measures to prevent abscesses in predisposed teeth. In this case, occlusal coverage with acid-etched composite resins probably would suffice.

It is interesting to compare this patient with her mother from whom she inherited the condition. The mother had no history of dental abscesses and radiographs (Fig 4) show no abnormalities except for caries. The pulp chambers appeared normal and in spite of the deep occlusal caries on the left mandibular first molar, no apparent abscess has developed.

### Grade III (Case 1)

The patient, a 10-year-old male, was referred to the University Dental School by his private practitioner at the age of 4 years because of multiple "spontaneous" dental abscesses. There was no family history of rickets. The patient was referred to a pediatrician. He was given vitamin D and oral phosphate supplementation beginning at about age 7. When the patient first was seen by one of the authors (WKS) at age 9, he showed skeletal signs of rickets with bowing of the legs and frontal bossing of the skull. His height was 132 cm (25<sup>th</sup> percentile) and he weighed 38 kg (90<sup>th</sup> percentile).

All immediate family members were healthy and the mother's medical history proved negative. It was



FIG 5. Periapical radiographs of the maxillary and mandibular anterior teeth of a male (Case 1) taken at initial examination. Note enlarged pulp chambers and periapical radiolucencies associated with the incisor teeth.

concluded that the patient's disease may be the result of a fresh genetic mutation.

When the patient first presented to the Dental School at the age of 4 years, all his primary incisors showed chronic draining abscesses. The teeth were not carious and there was no history of trauma. Radiographs showed extremely large pulp chambers and poorly calcified dentin (Fig 5). Histologic studies of the extracted teeth revealed large quantities of interglobular dentin and extensions of pulp chambers into the incisal edges of the teeth (Fig 6).

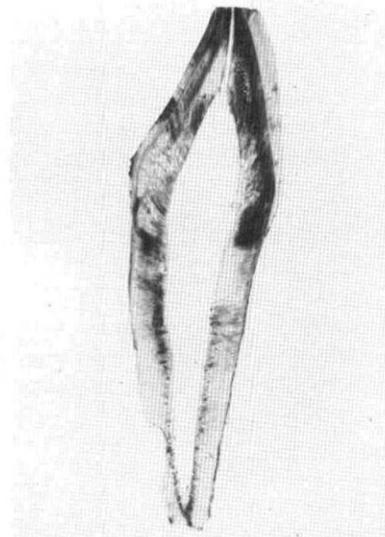


FIG 6. Section of a mandibular primary incisor from Case 1. Note the large size of pulp chamber, poorly calcified dentin (interglobular dentin), and extensions of the pulp chambers into the incisal edges of the teeth.

The abscessed incisors were extracted soon after the initial examination. On subsequent visits, acid-etched composite resins were placed over the occlusal surfaces of the remaining primary teeth in an attempt to prevent further pulp exposures and ab-

scesses. These resin caps were checked and adjusted regularly. However, in spite of this prophylactic procedure, all the remaining primary teeth subsequently became abscessed and required either extraction or endodontic treatment.

When the patient was seen by one of the authors (WKS) at 9 years of age, it was decided to use more aggressive methods to prevent abscesses in the permanent dentition. As soon as the first permanent molars erupted, the occlusal surfaces were capped with acid-etched composite resins. When the teeth erupted sufficiently, it was decided to cap them with stainless steel crowns. Because of the large pulp chambers (Fig 7) there was grave danger of pulp exposures if routine tooth preparation was undertaken. This problem was overcome by first placing separating elastics interproximally to open up contact areas between the teeth,<sup>16</sup> thus reducing the need for proximal reduction. Occlusal reduction was achieved by reducing the occlusal composite resin caps placed earlier. Prior to cementation of the stainless steel crowns, any enamel not covered by the composite resin was lined with calcium hydroxide before cementation with zinc phosphate cement.

When the permanent incisors erupted, the decision as to whether to cap these teeth had to be made. As the maxillary and mandibular incisors were contacting only minimally, it was decided that wear on these teeth would be slight and the need for protection not great. However, the lower right lateral incisor subsequently became abscessed and endodontic therapy was instituted. This forced the authors to review the decision not to cap the incisors and on later visits, the incisal edges of these teeth were protected with acid-etched composite resins.

At the time of writing, the first premolars were in the early stages of eruption. A plan of treatment similar to that for the first permanent molars was suggested and acid-etched composite resins were used to cap the occlusal surfaces of the first premolars that emerged. Stainless steel crowns for these teeth are planned as soon as the teeth have erupted into occlusion.

When the patient reaches adulthood, the stainless steel crowns should be replaced with full gold or porcelain bonded-to-gold crowns to increase fit and marginal adaptability.

## Discussion

This study of 13 patients with VDRR from several families illustrates the wide range of dental manifestations that are seen in this condition. These patients can be divided into 3 main grades according to the severity of dental signs: Grade I patients have minimal dental signs of the disease: Grade II patients usu-



FIG 7. Bite-wing radiographs of Case 1 taken at age 10 years. Note Grade III severity of dental manifestations with enlarged pulp chambers and abnormally calcified dentin.

ally show involvement of a few teeth only; and Grade III patients have severe dental manifestations such as multiple dental abscesses and grossly enlarged pulp chambers.

There are various factors which can account for the wide spectrum of dental manifestations in VDRR. First, genetic factors may play an important role in determining the severity of disease. It is apparent from this study that the severity of dental manifestations is similar within each family. For example, in 1 family (Cases 11-13), both the female patients and their affected mother show only minimal dental signs of VDRR. In another family (Cases 5 and 10), both affected mother and daughter exhibited mild dental manifestations of the disease. It is likely that VDRR is inherited in several different forms varying in severity, with each affected family showing similar severity among its members.

Within each affected family, individual variations may arise. An important factor is sex of the patient. Females tend to show less disease than males as expected of an X-linked trait. In females, partial protection is obtained from the presence of a normal X chromosome in addition to the X chromosome carrying the abnormal gene. Also, other factors such as hormones may influence the severity of disease in affected females. For example, it had been shown that there is no consistent correlation between the severity of hypophosphatemia and the severity of bone disease in females.<sup>3</sup> This present study, too, shows that dental signs are less severe in females. Out of 9 females, 7 can be classified into the group showing mild dental manifestations (Grade I), while the other 2 belonged to the group with moderate dental manifestations (Grade II). On the other hand, the 2 children showing the most severe dental manifestations (Grade III) are both males (Cases 1 and 2). Another male patient (Case 3) showed moderate dental findings while the fourth male patient (Case 9) had no history of dental abscesses and no increased sizes of the pulp chambers. However, because the latter patient was only 5 years of age at the time of dental examination, it is difficult to determine the extent of involvement of the permanent teeth. Pliskin and colleagues<sup>9</sup> reported a case of VDRR in whom only

**Table 1.** Characteristics of 13 Patients with Vitamin D-Resistant Rickets

Case	Sex	Age at Dental Examination (years)	Age of Diagnosis and Start of Medical Treatment	No. of Abscessed Teeth		Increased Size of Pulp Chambers	Hypoplasia of Teeth
				Primary	Permanent		
1. MG	M	10	4.5 yr	20	1	+++	+
2. SS	M	7	2 yr	16	3	+++	-
3. VB	M	25	2 yr	?	2	++	-
4. SB	F	32	2-3 yr	?	7	+	+
5. NS	F	13	18 mo	3	0	+	+
6. JS	F	25	<12 mo	?	1	-	-
7. KB	F	9	9 mo	0	0	-	+
8. AB	F	2	9 mo	0	-	?	-
9. MB	M	5	9 mo	0	-	+	-
10. WS	F	33	28 yr	?	0	-	-
11. JB	F	35	3 yr	?	0	+	+
12. CB	F	13	9 mo	0	0	-	+
13. TB	F	14	9 mo	0	0	-	-

the permanent dentition showed obvious clinical manifestations.

Medical therapy received by the patients may influence the severity of dental manifestations. Oral supplementation of inorganic phosphate to replace the abnormal renal losses of phosphate is the usual method of treatment in VDRR. In addition, vitamin D in the form of calcitriol also is given to prevent phosphaturia and hypercalcemia which may result from phosphate loading. In children with known family histories of the condition, diagnosis usually is made soon after birth. However, phosphate and vitamin D supplementation is not often given until at least after 9 months of age. This is because the low glomerular filtration rate in early infancy may prevent excessive losses of phosphate,<sup>1</sup> thus reducing the need for early phosphate supplementation. In addition, constant monitoring of serum levels is vital in vitamin D supplementation and repeated blood sampling is not feasible in the very young infant.

Oral supplementary phosphate and calcitriol should improve dental calcification and prevent abscesses. However, because many patients are not diagnosed and treated until after 2 years of age, the entire primary dentition and permanent incisors and first molars do not receive the beneficial effects of medical therapy, and are at greatest risk for developing dental abscesses. In this series, the 2 patients (Cases 1 and 2) with the greatest number of abscesses were both diagnosed and treated only after 2 years of age; in both cases, the entire primary dentition became abscessed. In contrast, another male patient (Case 9) who was diagnosed and treated at a few months of age still has not developed any abscesses of the primary teeth and the pulps of his teeth appeared fairly normal on radiographs.

The results of this study (Table 1) indicate that with the exception of a mildly affected female (Case 10) who was not diagnosed until 28 years of age, the

earlier the institution of medical therapy, the less severe the dental manifestations. Further longitudinal clinical as well as histological studies on teeth need to be performed to establish the importance of medical therapy on dental calcification in VDRR.

Prevention of dental abscesses is an important aim in dental management of VDRR. Even minimal wear of the teeth can result in pulp exposures and protection of functional tooth surfaces should be considered. The need for such prophylactic coverage varies with the severity of dental manifestations.

Besides prophylactic coverage to prevent occlusal wear, routine preventive care for dental caries is extremely important as minimal caries can lead to pulp exposures. Fluoride therapy, dietary advice, and oral hygiene therapy should be given regularly.

Besides prophylactic treatment, control of existing infection is important in the dental management of the patient with VDRR. Most clinical studies report success with routine endodontic procedures for abscessed teeth in VDRR. However, the thin and poorly calcified dentin walls of the root canals do not allow excessive instrumentation and care has to be taken to prevent perforation and root fracture. Also, if abscessed primary teeth are extracted, considerations must be given to space maintenance.

## Conclusions

The dental manifestations seen in patients with VDRR appear in a spectrum of severity, ranging from the very severe, with involvement of nearly the entire dentition, to the very mild with normal appearance of the teeth. Effective strategies for the prevention of dental abscesses are available and should be employed to suit each individual patient's needs.

Dr. Seow is a pediatric dentistry lecturer, University of Queensland, and Dr. Latham is deputy medical superintendent, Royal Children's Hospital, Herston, Australia. Reprint requests should

be sent to: Dr. W. Kim Seow, Dept. of Social and Preventive Dentistry, University of Queensland, Turbot St., Brisbane, Australia 4000.

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