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What is This?
Inhibition of Tooth Development with a Sclerosing Agent, Sodium Tetradeyl Sulfate

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SYNOPSIS IN INTERLINGUA

INHIBITION DEL DISVELOPPAMENTO DENTAL PER UN AGENTE SCLEROTISANTE (SULFATO TETRACLYC DE NARIUM).—Le tertie e quarte premolares in stato evolvente de 15 canes hybrida esseva tractate con injectiones de 0,3 ml de un solution de 3 per cento de sulfato tetradeyl de natrium alternatemente al lateres sinistre e dextere. Un sterile solution salin esseva injicite pro objectivos de controlo ad in le dentes contralateral.

Examines radiographic revelava le complete inhibition del eruption del dentes. Tamen, un latente sed atrophi disveloppamento de radices esseva notate in tres dentes.

Histologicamente, responsas pulpal de inflammation sequite del formation secundari de dentina e osso si ben como responsas de degeneration ameloblastyc, de invasion ossee, e de resorption de adamantine in organos adamantin esseva observate.

Various potentially undesirable teeth develop in the jaws and should be eliminated for prophylactic reasons; these include teeth that are impacted, supernumerary, or are to be removed for orthodontic purposes. At present, the most efficient manner of eradicating these teeth is by surgical excision. It was postulated, however, that if these teeth could be inhibited at an early stage of development, a resorptive process would occur. Thereby, a conservative means to eliminate such teeth would be provided.

In this investigation, the hypothesis was tested by injecting a sclerosing agent, sodium tetradeyl sulfate,† into the developing teeth of mongrel dogs. It was expected that this would yield information that eventually could be applied to the conservative elimination of undesirable teeth in man.

The selection of sodium tetradeyl sulfate as the sclerosing agent of choice was made after an extensive review of the litera-

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† Sotradecol®, also referred to as S.T.S., Philadelphia Ampoule Laboratories, Philadelphia, Pa.

Materials and Methods

Fifteen mongrel dogs, 8 to 10 weeks old, were used in this study. They were anesthetized with ether before being surveyed radiographically, and the location of the crypts and teeth of the permanent third and fourth premolars was determined. Intra-bony injections were then made with blunted 20-gauge needles through holes drilled with tapered bevel burs of comparable size. Three-tenths milliliter of 3 per cent buffered sodium tetradeyl sulfate was injected into each crypt, alternating right and left sides of the mandible in each dog. The opposite sides served as controls; 0.3 ml of physiologic saline solution was injected. This procedure was repeated after 2 weeks, and radiographs were taken every 2 weeks thereafter.

The dogs in this study were allotted to two groups. Group I dogs were sacrificed at intervals of 1, 2, 3, 4, 5, 6, 7, and 14 days after the first injection, and Group II dogs were sacrificed at 1, 2, 4, 8, 12, 16, and 20 weeks after the second injection. After
sacrifice, sections of the mandible containing the teeth under study were fixed in 10 per cent formalin.

Decalcification was carried out with ethylenediaminetetraacetic acid (EDTA). Tissue sections were cut at 10 μ and stained, using hematoxylin and eosin stain and Mallory's connective tissue technic.

Results

The results were assessed radiographically and histologically. A radiographic survey was made in each dog, but results were interpreted only for 6 dogs in Group II sacrificed at 2, 4, 8, 12, 16, and 20 weeks following the second injection. This was because the earliest stage at which these results could be consistently interpreted radiographically was 2 weeks after the second injection, or 4 weeks after the first injection had been given.

Radiographic Results.—The two primary interpretations made from the radiographs concerned (1) growth and development and (2) rate of eruption of the developing teeth.

The effect of the injected solutions on growth and development was interpreted as complete, partial, or no inhibition. The method of analysis used was the radiographic comparison of the growth and development of experimental with control teeth. Of the total of 12 experimental teeth in 6 dogs, 9 exhibited complete, and 3 partial, inhibition of growth and development (Fig. 1D, 2B, 3B). The teeth with partial inhibition each exhibited aberrant shortened root formation of one root (Fig. 2B, 3B). Ten of the 12 control teeth exhibited normal progressive growth and development with no demonstrable inhibitory effects (Fig. 2D). Two control teeth exhibited generalized underdevelopment or microdontism with malformation of the crowns and roots (Fig. 3D).

The effect of the injected solutions on eruption was assessed as no inhibition or complete inhibition. The method of analysis used was the comparison of eruption of experimental with control teeth. Observations were made only on the 3 dogs in Group II in which the eruption actually took place. The teeth treated with sodium tetradecyl sulfate exhibited complete inhibition of eruption, including those teeth with aberrant root formation. All 6 control teeth, including those manifesting microdontism, exhibited normal progressive eruption; no inhibitory effects observed (Fig. 2D, 3D).

Fig. 1.—Dog sacrificed 4 weeks after the second injection. (A) Left premolar prior to the first injection of saline solution. (B) Four weeks after the second injection of saline solution; normal development. (C) Right premolars prior to injection of sodium tetradecyl sulfate. (D) Four weeks after the second injection of sodium tetradecyl sulfate. Development of both premolars is inhibited and there are sclerotic changes in the teeth and surrounding bone. (Orig. mag. X2.5.)
Fig. 2.—Dog sacrificed 12 weeks after the second injection. (A) Left premolars prior to first injection of sodium tetradecyl sulfate. (B) Twelve weeks after the second injection of sodium tetradecyl sulfate. Notice retained deciduous teeth, inhibition of eruption and development of both premolars, and aberrant development of distal root of third premolar. (C) Right premolar prior to the first injection of saline solution. (D) Twelve weeks after the injection of saline solution. Notice the normal eruption and deformities in crowns. (Orig. mag. X2.5.)

Fig. 3.—Dog sacrificed 20 weeks after the second injection. (A) Left premolars prior to the first injection of sodium tetradecyl sulfate. (B) Twenty weeks after the second injection of sodium tetradecyl sulfate. Notice the inhibition of eruption and development of mesial root of the third premolar. (C) Right premolars prior to the first injection of saline solution. (D) Twenty weeks after the second injection of saline solution. Notice the eruption of control teeth with microdontia and malformation of crowns and roots.
An increase in density and partial obliteration of the treated teeth and surrounding bony trabeculae were interpreted as a sclerotic change (Fig. 1D, 2B). These changes appeared 2 to 6 weeks after the second injection of sodium tetradeyl sulfate. Careful observation of the radiographs revealed that the bony architecture returned to its finely trabeculated pattern and appeared normal after 10 to 12 weeks in the dog sacrificed at 16 weeks, after 12 to 14 weeks in the dog sacrificed at 20 weeks (Fig. 3B). These were the only 2 dogs maintained long enough to illustrate this effect. This information was later verified histologically.

Root resorption of the deciduous premolars was observed to occur within 6 to 10 weeks after the second injection (Fig. 2B). Eruption of the succedaneous teeth took place within a few days after exfoliation of their deciduous predecessors.

Radiographically, the teeth adjacent to those treated with sodium tetradeyl sulfate did not appear to be affected on either side of the mandible.

Histologic Results.—Histologic studies were performed on all 15 dogs, or a total of 60 treated teeth. Histologically, a generalized pattern depicting the effect of the sclerosing agent was apparent, but a series of progressive reactions could not be seen in specimens collected at measured intervals of time. In Group I, the pulp generally exhibited inflammation, leukocytic and lymphocytic invasion, necrosis, odontoblastic degeneration, pulpal condensation, and extravasation of blood. Isolated cases of pulpal abscess formation, fibrosis, and thrombosis were also observed. The enamel organ generally exhibited leukocytic and lymphocytic invasion, inflammation, ameloblastic degeneration, and extravasation of blood. Cyst formation was noted in 1 tooth.

In Group II, after the second injection of sodium tetradecyl sulfate, the dog sacrificed at 1 week had a response similar to that described for Group I. The findings in the remaining 6 dogs, with a total of 12 experimentally treated teeth, could be grouped into three categories. The predominant pulpal features of the different categories consisted of (1) odontoblastic degeneration, ectopic bone formation (Fig. 4, 4A), and pulpal fibrosis; (2) no odontoblastic degeneration, excessive deposits of secondary dentin, and pulpal atrophy (Fig. 5); and (3) aberrant stunted root formation and pulpal fibrosis. The enamel organ response of the specimens in Group II presented a picture of ameloblastic degeneration, bone invasion, and enamel resorption (Fig. 4, 4B).

The control teeth of Group I and II dogs exhibited an inflammatory response at the site of the injection. This was followed by a reparative phase of fibroblastic proliferation and osteogenesis.

The previously mentioned sclerosis of the surrounding bone observed radiographically was interpreted as being due to hypercalcification, since no specific increase in bone density was seen histologically. In addition to the factor of hypercalcification of the overlying bone, ectopic bone formation (Fig. 4) and secondary dentin formation (Fig. 5) within the pulp chamber of the developing tooth further contributed to the obscuring of the developing tooth on the radiograph.

Conclusions

The use of sodium tetradecyl sulfate in the inhibition of developing teeth certainly must undergo more extensive investigation. Information obtained from this investigation warrants the following conclusions, however.

1. No toxic systemic manifestations were produced by sodium tetradecyl sulfate injected into the developing teeth of mongrel dogs. This information is in keeping with previous findings associated with the clinical usage of this drug.

2. Generally, sodium tetradecyl sulfate did not produce local reactions, but localized abscess formation was observed at the site of one injection. It was concluded that this abscess was the result of an infection superimposed on, and exacerbated by, the inflammatory condition produced by the sodium tetradeyl sulfate.

3. The eruption of all the developing teeth treated with sodium tetradeyl sulfate was inhibited.

4. Sodium tetradeyl sulfate appeared to inhibit growth and development in most of the treated teeth. The drug was not completely effective, however, as was evident in 3 teeth with aberrant shortened or stunted root formation in one root each. This was ascribed to the failure of the drug to completely inhibit all of the specific growth cen-
Fig. 4.—Third premolar of a 4-week specimen. (Orig. mag. X15.) (A) Osteoclastic resorption of enamel. (Orig. mag. X160.) (B) Dentin (1); bony invasion (2); exophytic bone growth (3), and entrapped necrotic debris (4). (Orig. mag. X40.)

ters of the roots. Thus, the roots developed, but in an abnormal manner.

5. The injection of normal saline solution did not affect the growth and development in 10 of the control teeth observed. It may be postulated that the two cases of generalized underdevelopment, or microdontism, with concomitant abnormalities in tooth structure were due to injuries of the growth centers caused by the trauma of drilling. No definite conclusions can be drawn on the basis of this limited study, however.

6. Sodium tetradecyl sulfate produced radiographically interpretable sclerotic
changes in the tooth and in the bone immediately surrounding the involved tooth. The sclerosis of the bone was reversed and architecture appeared normal after 10 to 12 weeks.

7. Histologically, a generalized pattern depicting the effects of the sclerosing agent was apparent, but a graded series of progressive changes could not be seen in one dog and the next. Initially, an acute inflammatory response was produced when sodium tetradeeyl sulfate was injected into the tooth. The histologic patterns then stabilized and illustrated chronic inflammation for a period. The pulp responded to the drug in an erratic manner by forming secondary dentin or ectopic bone within the pulp, or layers of bone and dentin in the walls of the developing teeth. The enamel organ presented a picture of ameloblast degeneration, bone invasion, and enamel resorption. Sections taken from control teeth exhibited only the normal processes of healing and repair.

8. It may be concluded from the collected evidence that the changes in the developing teeth were due to the sclerosing agent, sodium tetradeeyl sulfate, and not to piercing the tooth by a bur or the injection of a fluid.

Discussion

It is believed that the primary factor in the inhibition of the developing teeth was the interference of the sodium tetradeeyl sulfate with the nutritive blood supply. It is well known that the growth and viability of all tissues are directly dependent on an adequate vascular supply. Neoplasms have been known to regress spontaneously due to ischemia produced by blockage of local circulation. Furthermore, Shultz has reported several cases of ameloblastomas regressing in size after injections with a sclerosing solution. Thus, the hypothesis may be made that sodium tetradeeyl sulfate reduced the local blood supply of the developing tooth, thereby causing inhibition of growth and development. In fact, the varying degrees of inhibition that occurred probably could be directly correlated with the residual vascular supply of the tooth in question. These hypotheses cannot be proved, however, by the limited histologic studies carried out in this investigation. Additional experimentation along other lines must be performed.

Other factors playing an important role in the inhibition of tooth development are the stage of development at the time of injection, site of injection, and the per cent and volume of sodium tetradeeyl sulfate injected. Although the concentration required for inhibition of development was predetermined by pilot studies, further studies may yield a more effective dosage.

Experimentation presently is being performed on teeth at an earlier stage of development. Thus, the sodium tetradeeyl sulfate will be allowed to exert its maximum inhibitory effect prior to the maturation of growth centers in the root region. If the tooth is inhibited at this earlier stage of development, the possibility of complete atrophy and resorption of the residual enamel and dentin will be enhanced. From preliminary observations, a high per cent of successful results is anticipated.

Finally, it may be noted that sodium tetradeeyl sulfate has been in use since 1946 by the medical profession, but it has not as yet gained acceptance in the armamentarium of dental therapeutics, although this drug has greater efficiency and lower toxicity and causes minimal allergic manifestations and less tissue reactions than the
sclerosing agents in more common usage. At present, the only clinical study known to have been performed using sodium tetradecyl sulfate in the oral cavity deals with the sclerosing of hemangiomas. As the dental profession becomes better acquainted with sodium tetradecyl sulfate, it is believed that this drug will rapidly replace those presently in use as sclerosing agents.

Summary

Sodium tetradecyl sulfate was selected as the sclerosing agent of choice and the effect of this drug on tooth development in 15 mongrel dogs was studied. The dogs were allotted to two groups and given one or two injections of sodium tetradecyl sulfate in predetermined teeth. Injections were made in 60 teeth, 2 injections of sodium tetradecyl sulfate and 2 of normal saline solution in each dog. The dogs were sacrificed at intervals from 1 day to 20 weeks. Radiographic and histologic studies were subsequently performed. Sodium tetradecyl sulfate, as employed in this experiment, was not completely effective in inhibiting the development of all of the injected teeth. Further studies have been suggested from which more favorable results are anticipated.

References