The effect of systemic disorders on the dental pulp in experimental animals


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Pulpal conditions were studied in Chinese hamsters with hereditary diabetes mellitus, H-1-virus-modified hamsters, mice of the gray lethal mouse strain, polyoma-infected Swiss mice, mutation-diabetic mice, and rats with streptozotocin-produced diabetes. Degenerative pulpal changes in the Chinese hamsters and the polyoma-infected Swiss mice were often found in association with periodontal disease. While periodontal disease was found in the gray lethal mouse strain, little evidence of pulpal disease was noted. Some isolated teeth with pulpal changes were found in both the H-1-virus-modified hamsters and the polyoma-infected Swiss mice. Vascular alterations were found in the pulps of many of the mutation-diabetes mice, ranging from essentially normal to severe vascular engorgement with thrombosis. No alterations were found in either the periodontium or the pulps of the streptozotocin-diabetic rats.

Pulpal alterations have been described in a variety of systemic and genetic disturbances in experimental animals. Pulpal conditions were investigated in the following animals: (1) Chinese hamsters with hereditary diabetes mellitus, (2) H-1-virus–modified hamsters (3) mice of the gray lethal mouse strain, (4) polyoma-infected Swiss mice, (5) mice with mutation diabetes (an inbred mouse strain, C 57BL/Ks), and (6) rats with streptozotocin-produced diabetes.

PULPAL CONDITIONS
Chinese hamsters with hereditary diabetes mellitus

Approximately 200 Chinese hamsters (Cricetulus griseus) with hereditary diabetes were studied.1,2 The duration of the diabetic state ranged from 29 days to 14 months. All diabetic animals received insulin replacement therapy. Severe

1 Presented at the annual meeting of the American Association of Endodontists, Dallas, Texas, April, 1973.
Fig. 1. Second and first mandibular molars in a diabetic Chinese hamster with complete necrosis of both dental pulps due to caries. Periodontitis is also evident with bone resorption, cementum resorption, and gingival recession. (Hematoxylin and eosin stain. Magnification, x100.)

Fig. 2. First mandibular molar in diabetic hamster. Total necrosis of pulp resulting from caries and apical abscess is evident. Bifurcation involvement has resulted from periodontitis. (Hematoxylin and eosin stain. Magnification, x100.)

Periodontal involvement was noted in the Chinese hamsters which developed diabetes shortly after weaning. The periodontal involvement was characterized by pocket formation, inflammation, and alveolar bone resorption (Fig. 1).

In the diabetic animals with periodontal involvement, the pulps of many molars presented generalized atrophy. In teeth affected by caries the pulp was usually partially or completely necrotic, with severe inflammatory changes that were acute in nature. Pulpal abscesses were occasionally found in carious teeth where there was no obvious pulpal exposure, and apical abscesses often resulted from the pulpal involvement (Fig. 2). In the teeth uninvolved by caries, the pulp demonstrated varying degrees of degenerative alteration. The nuclei of the odontoblasts and pulpal fibroblasts were pyknotic and the cellular membranes were indistinct (Figs. 3 and 4). The odontoblastic layers in many teeth were no longer well defined. The pulpal ground substance was coarsely granular. Similar changes were seen in the incisor teeth, with severe cellular degeneration.

The pulpal involvement in the Chinese hamster with spontaneous hereditary diabetes often appeared to be secondary and was found in association with severe periodontal disease.
H-I-virus-modified hamster

Experimental production of craniofacial and dental deformities was first reported by Toolan. No tumors developed in hamsters injected at birth with fractions of cell-free filtrates of eight transplantable human tumors or with livers, spleens, and other tissues derived from human beings and rats carrying spontaneous cancers. Subsequent research revealed the causative agent to be a virus with osteolytic potential exerting a particular effect on the developing teeth and skeletal system. The H-1-virus-modified hamster is characterized by the following unusual features: (1) a small, flat face, (2) a microcephalic type of head, (3) protruding eyeballs, resembling exophthalmos, (4) protruding, large, smooth tongue, (5) abnormalities of the incisor teeth, consisting of either absence or extensive overgrowth in coil fashion, so that penetration of the labial mucosa occurred, (6) docility and easy management, (7) small size and weight, and (8) normal-appearing fur. The maxillary and mandibular molar teeth presented a variable pattern of structural and developmental abnormality. The periodontal membrane of the incisors appeared to be atrophic. The dental pulps in many molar teeth presented degeneration of the odontoblasts and pulpal fibrosis (Fig. 5). There was also some pulpal necrosis, and necrotic dentin often
undergoing resorption and replacement by connective tissue. The pulpal changes observed in hamsters injected with cell-free filtrates of human and animal tumors do not appear to be related to periodontal disturbance but rather to severe alterations and arrest in craniofacial and dental development.

**Mice of the gray lethal mouse strain**

The gray lethal mouse strain, a mutation of the house mouse (*Mus musculus* L), was originally described by Gruneberg. Gray lethal breeder animals (gl/+), produce offspring with one of three genotypes: (1) normal animals (+/+), (2) heterozygous (gl/+), carriers of the mutant gene, and (3) homozygous recessive animals (gl/gl) which exhibit the lethal character of the mutation. Phenotypically the homozygous normal (+/+), and the heterozygous carrier of the gene (gl/+) are indistinguishable. In trying to breed (gl/gl) gray lethal mice, Sheehan, Cohen, and Shklar found that they had bred a large colony of (+/+) normal animals and (gl/+) gray lethal carriers. They subjected the (gl/+) animals to various stresser agents and found that many of the animals manifested an apparent genetic susceptibility to periodontal disease. Although periodontal disease was present in the gray lethal strain mouse, they found little evidence of pulpal disease in several hundred animals studied (Fig. 6).

**Polyoma-infected Swiss mice**

Polyoma virus, originally isolated from leukemic mice, was found by Gross to be capable of inducing malignant tumors in experimental animals. Carcinomas
of the parotid glands were the most commonly observed of a large variety of
malignant lesions of both epithelium and connective tissue. Because of this
particular relationship, the polyoma virus was first referred to as the "parotid
tumor agent." The term polyoma was eventually utilized to indicate the ability
of this agent to produce many different types of malignancy in different tissues.

In addition to the interesting findings in the area of carcinogenesis, the
polyoma virus was found also to have striking effects upon the periodontal and
pulpal tissues of experimental animals, such as mice. Periodontal involvement in
polyoma-infected mice was found by Fleming and Soni* and severe periodontitis
was described by Cohen and Shklar.10 Among the changes described were ex-
tensive apical migration of epithelial attachment with periodontal pocket for-
mation, suppuration from the periodontal lesion, calculus deposition, and re-
sorption of interseptal and interradicular alveolar bone.

Pulpal changes were also described in noncarious teeth of polyoma-infected
animals. Varying degrees of odontoblastic degeneration and inflammatory in-
filtration were noted in the pulp chambers of noncarious teeth and severe
necrosis and abscess formation were observed in the dental pulps of teeth with
deep carious lesions or carious exposures.

In a later study Shklar and Cohen11 made observations on 50 Swiss mice
infected at birth with small doses of polyoma virus and put to death at varying
periods ranging from 6 months up to 12 months. Those animals developing
tumors were killed at 6 to 8 months. Non-tumor-bearing animals were killed
at 12 months. Immunofluorescence was the technique utilized for the detection of

Fig. 6. First mandibular molar tooth in gray lethal strain mouse showing periodontal
disease. There is migration of epithelial attachment, gingival recession, bone loss, and
calculus deposition. Dental pulp presents vascular dilatation but normal odontoblastic layer.
(Hematoxylin and eosin stain. Magnification, x100.)
polyoma viral antigen in the tissues of infected mice. Twenty-five Swiss mice uninjected with virus were used as controls and killed at ages similar to those of animals in the experimental group. In the experimental animals the dental pulps presented a variety of patterns, ranging from essentially normal to complete necrosis. In several animals with severe periodontal involvement the dental pulps were characterized by varying degrees of cellular degeneration and inflammatory infiltration. These animals were omitted from the study, since the pulpal alterations could represent an extension of the severe periodontal inflammation through apical involvement of the root canals from the adjacent deep periodontal pockets.

The parotid malignancies in these animals were adenocarcinomas. In general, the incidence of pulpal and periodontal disease did not relate to the presence of parotid tumors nor was the severity of the pulpal and periodontal involvement related to the size of the tumors.

In animals with minimal or moderate periodontal involvement, there were varying degrees of pulpal pathosis. Most observations were made on the dental pulps of the mandibular first molars, although pulps of other teeth were also studied. In several animals the pulp was essentially normal, with a regular
odontoblastic layer of cells and evenly spaced pulpal fibroblasts lying within
a loose myxomatous connective tissue stroma. Infiltration of lymphocytes was
minimal but was frequently observed in these cases. In other animals the pulps
were relatively normal in cellular architecture but the loose connective tissue
was replaced by a dense fibrous variety and more inflammatory cells were
evident. A more severe alteration was noted in several of the polyoma-infected
animals. The odontoblastic layer was destroyed, so that the cells contained
pyknotic nuclei. Pulpal blood vessels were dilated and engorged with erythro-
cytes, while dense inflammatory infiltration was noted within the pulp proper.
The pulpal fibroblasts also presented degenerative changes (Fig. 7).

In teeth involved by deep caries or carious exposure, the entire dental pulp
was necrotic, with some inflammatory cells appearing in the apical portions of
the root canals. The pathosis often spread to involve the periapical area or the
bifurcation area. An acute abscess developed in these involved tissues, resulting
in resorption of alveolar bone and cementum. The abscesses tended to be well
circumscribed, whether in the apical periodontium, the bifurcation area, or
the gingiva. Where the pulp exposure was small or not easily seen, the pulp
merely demonstrated hemorrhagic necrosis. However, where the opening was
obvious and the carious destruction extensive, the pulp was filled with dense
masses of necrotic tissue.

**Mice with mutation diabetes (an inbred strain characterized by a metabolic
disturbance resembling diabetes)**

Hummel, Dickie, and Coleman\(^\text{12}\) inbred a strain of mice, autosomal recessive
in character, which manifested diabetes mellitus. Between the third and fourth
postnatal weeks the mouse developed obesity which was followed by hypergly-
cemia, polyuria, and glycosuria. Histologic study of the pancreas showed some
morphologic changes in the islets of Langerhans which may have reduced the
production of insulin. The kidneys, adrenals, retinas, thyroid, and lungs of these
animals presented no gross pathology. Histologic observations were made on
the dentitions and periodontal structures of 50 of these animals.\(^\text{13}\) The animals
studied were killed at periods varying from 26 days to 56 weeks. The “diabetic”
mice presented little evidence of periodontal disease but vascular alterations
were noted in the dental pulps of many of them. The epithelial attachment of the
gingiva was usually at the cementoenamel junction (Fig. 8). Occasionally, slight
migration of the epithelial attachment was noted, but no periodontal pocket
formation was observed. The dental pulps presented alterations ranging from
essentially normal to severe vascular engorgement with evidence of thrombosis
(Figs. 8 and 9) and some thickening of capillary walls. The odontoblastic layer
appeared to be intact and essentially normal.

**Rats with streptozotocin-produced diabetes**

Sixty male and female albino rats of the Wistar strain were rendered
diabetic with streptozotocin.\(^\text{14}\) Streptozotocin is a broad-spectrum antibiotic
which has been proved to have a diabetogenic potential. It has been shown to
have antitumor as well as tumorigenic properties. In these animals the islets
Fig. 8. Maxillary and mandibular molars in “diabetic” mouse. Periodontal tissues are normal. (Hematoxylin and eosin stain. Magnification, ×50.)

Fig. 9. High-power view of dental pulp in Fig. 8 showing enlarged vessels with thrombosis. (Hematoxylin and eosin stain. Magnification, ×200.)

of Langerhans are reduced in size and number with some degeneration of the beta cells. The animals were given a single dose of intravenous streptozotocin (65 mg. per kilogram) and 48 hours after injection the animals manifested hyperglycemia, polyuria, and glycosuria. Animals that survived 120 days or longer were killed. No alteration in either the periodontium or pulp in rats rendered diabetic with streptozotocin was observed.

DISCUSSION

A clinical entity, the “pulpodontic-periodontic syndrome,” has recently been suggested. This syndrome may be of pulpal or periodontal origin. In a clinical and histologic study of human, dog, and monkey teeth, they demonstrated that pulpal disease may aggravate periodontal disease and periodontal disease is capable of causing pulpal disease. Observations on monkey and dog teeth in the same study with induced pulpal lesions produced inflammatory changes in the periodontal ligament without pocket formation.

Bender and Seltzer also suggested that the effect of periodontal disease on the pulp was based on anatomic and circulatory interrelationships. In the present study we found some isolated teeth with pulpal changes in both the
H-1-virus-modified hamsters and in the polyoma-infected Swiss mice. It was not surprising to find some pulpal changes in the H-1-virus-modified hamsters since there was such gross developmental abnormality of the head, with interference of craniofacial and dentofacial development, resulting in abnormal dentin and root formation.

The isolated pulp changes in the polyoma-infected Swiss mice may be attributed to the overwhelming infection of the animal reducing the inherent natural defense mechanism of the pulp. The blood vessel changes in the mutation diabetic mouse is of interest and requires further study. In the present study the pulpal changes in the Chinese hamster, the gray lethal mouse strain, and the polyoma mouse were often found in association with periodontal disease.

SUMMARY

Pulpal conditions were studied in the following experimental animals: Chinese hamsters with hereditary diabetes mellitus, H-1-virus-modified hamsters, mice of the gray lethal mouse strain, polyoma-infected Swiss mice, mutation-diabetic mice, rats with streptozotocin-induced diabetes.

Degenerative pulpal changes in the Chinese hamsters and the polyoma-infected Swiss mice were often found in association with periodontal disease. While periodontal disease was found in the gray lethal mouse strain, little evidence of pulpal disease was noted.

Some isolated teeth with pulpal changes were found in both the H-1-virus-modified hamsters and the polyoma-infected Swiss mice. Pulpal changes in the H-1-virus-modified hamster are probably due to the gross developmental abnormalities of the head, with interference of craniofacial and dentofacial development, resulting in abnormal dentin formation. Pulpal changes in the polyoma-infected Swiss mouse are probably due to the overwhelming infection of the animal reducing the inherent natural defense mechanism of the pulp.

Vascular alterations were found in the pulps of many of the mutation-diabetic mice. The pulps presented alterations ranging from essentially normal to severe vascular engorgement with thrombosis. No alterations were found in either the periodontium or the pulps of the streptozotocin-diabetic rats.

REFERENCES

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