Review

Induced and Spontaneous Lesions in Teeth of Laboratory Animals

Klaus Weber

RCC Ltd., Zelgliweg 1, 4452 Itingen, Switzerland

Abstract: Tooth lesions may be either spontaneous or induced in nature. Such lesions may be acquired by trauma or iatrogenic mechanically induced. Examples are mechanically induced lesions at a high incidence in mice of an oncogenicity study and induced tooth lesions in dogs out of pulp-dentin test studies. In contrast, chemically induced lesions may be also recorded. There are examples discussed in rats of an oncogenicity study induced by a compound acting on the vasotogenous, as well as in mice of a subacute toxicity study induced by a fluorinated compound. Also neoplasia may be recorded, that may be induced by chemical products, or intrinsic as genetical background lesion, or even in some rare cases spontaneous in nature. The incidence and types of spontaneous odontogenic neoplasia is discussed for rats, mice including transgenic mice (Tg.AC), and dogs.

Key words: spontaneous tooth lesions, induced tooth lesions, odontogenic neoplasms

Introduction

Tooth lesions are rarities in laboratory animals. An overview on lesions of the rat incisor is published elsewhere. The incisor morphology reflects the nutritional status of the animal. There may be fluctuations of mineral metabolism and the rodent incisors due to life-long growing disclose vitamin availability affecting the rat incisor. Also metals may be involved in incisor pathology. Cadmium-induced changes were described along with decreasing iron-containing pigment in ameloblasts leading to the loss of incisor coloration and destruction of ameloblasts as well as necrosis of the dental pulp were described. Furthermore, hormonal disturbances may give rise to typical structural alterations of the incisor in the laboratory animal. A direct relationship between anomalies and parathyroid hormone related peptide and its receptor PTHR1 axis were recently suggested. Certain chemicals may have deleterious effects upon the odontogenic tissues, resulting in tooth deformation and malocclusion and eventually in odontomas. Amongst the chemical compounds leading to morphological changes in rodent teeth, there are various antitumor drugs i.e. 5-fluorouracil, adriamycin, mitomycin C, vinblastine sulphate, taxotere, irinotecan hydrochloride, or cisplatin causing a variety of dental lesions that vary temporally and spatially, macrolide antibiotics increasing the number degenerating ameloblasts and impaired iron pigment secretion at the pigmentation stage, tetracycline affecting the enamel organ, phosphonate compounds affecting the dentin and enamel due to hypomineralization, 2-butoxyethanol causing dental pulp thrombosis, pulp infarction, and odontoblast infarction, or hexachlorobenzene leading to focal mesenchymal cell vacuolation and focal osteodentin formation within the pulp, odontoblast degeneration and formation of dentin niches.

Material and Methods

All samples fixed in phosphate-buffered 4% formaldehyde were decalcified in formic acid, processed, embedded in paraffin, cut at an approximately thickness of 5–6 µm, and stained by hematoxylin and eosin.

Oncogenicity (inhalation) study in CD-1 mice

Tissue samples of early decedents of a 104-Week inhalation (nose only) oncogenicity study, including those of control animals receiving air that were found dead or were sacrificed due to poor health during the first 2 weeks were examined.

Pulp-dentin test in Beagle dogs

In a pulp-dentin compatibility study, standardized class V box cavities with all margins in enamel were prepared on the buccal surface of premolars or molars without exposure of the pulp. Negative control cavity floors were lined with RelyXTM Temp E and covered with FiltekTM Z250 after pre-treatment with a self-etch adhesive (Prompt-L-Pop)
according to manufacturers instructions (in many other studies, the cavities are simple with amalgam). Positive control cavities were filled with silicate cement (Zhanelka® Silikatzement). In teeth of each dogs, there were also test item filled cavities. Interim sacrifices were performed at 7, 28 and 42 days.

**Oncogenicity (feeding) study in Wistar han: RCC rats, compound acting on vasotonus**

Decedents of a 104-Week oncogenicity study in Wistar Han: RCC rats of approximately 6–8 months after study start were examined. Control animals received the diet without the test item.

**28-Day (gavage) study in Sprague Dawley rats, fluorinated compound**

Samples from a 28-day oral (gavage) study with a 14-day recovery period were examined. The animals received the test item once daily by gavage. Control animals received the vehicle, 1% Tween 80 in distilled water.

**Neoplasms in rats, mice and dogs**

Spontaneous neoplasms of rats were selected from studies at RCC performed in Wistar Han: RCC rats, whereby only one compound odontoma was recorded amongst control animals. Neoplasms from mice were all selected from a bioassay with transgenic mice (Tg.AC). A single case of an ameloblastoma of a dog (unknown breed and age) is presented.

**Results**

**Oncogenicity (inhalation) study in CD-1 mice**

The cause of morbidity in early decedents was related to purulent renal inflammations along with tooth lesions in a high percentage of the respective animals. In teeth, histopathological lesions consisted of inflammatory and reactive lesions. Vascular dilatation within the pulp cavity, often along with thrombosis and fibrosis were recorded (Fig. 2). The loss of odontoblasts was accompanied by the formation of dentin niches (Fig. 3) and focally or multifocally thinner dentin layers. In other samples, there was also dentin layer thickening due to apposition of immature basophilic dentin (Fig. 4). Often, within the pulp focal thrombosis and fibrosis became replaced by osteodentin. In some teeth, there was a subacute to chronic periodontal and/or root inflammation (Fig. 5). Rarely, fragments of fractured teeth could be recorded within alveoli that partially were replaced by mesenchymal tissues (Fig. 6). Occasionally, the formation of an abscess within the pulp was recorded (Fig. 7). In other rare cases, the tooth damaged mechanically the nasal bone by breaking through the alveolar bone leading to an acute to subacute inflammation of the adjacent tissues (Fig. 8). Animals that survived a longer period showed dentin dysplasia characterized by an irregular mass of dentin-like material blocking the pulp cavity completely or forming so-called denticles only (Fig. 9).

**Pulp-dentin test in Beagle dogs**

In single cases of negative control treated teeth, there was pulp congestion, pulp necrosis and acute to subacute inflammation. Similar lesion but of a higher severity characterized by chronic granulomatous inflammation and fibrosis were recorded in the tooth pulp of teeth treated with the positive control (Fig. 10).

**Oncogenicity (feeding) study in Wistar han: RCC rats, compound acting on vasotonus**

Histopathological lesions in teeth consisted of vascular dilation within the pulp cavity along with congestion, again often along with thrombosis (Figs. 11, 13) and fibrosis. The partial or complete loss of odontoblasts was accompanied by the formation of dentin niches (Fig. 12) and thinning of dentin layers or, in some cases apposition of a more basophilic dentin (Fig. 13). In several cases, abberant dentin was recorded within the pulp regarded to be an early stage of dentin dysplasia (Fig. 14). In other cases, there was thrombosis and/or fibrosis in within the pulp cavity occasionally replaced by osteodentin or bone (Fig. 15). In addition, in several samples there was a rarefaction of ameloblasts (Fig. 16). There were also cases of dental dysplasia characterized by the complete replacement of the authentic tooth by irregular masses of dentin-like material.

**28-Day (gavage) study in Sprague Dawley rats, fluorinated compound**

The most significant macroscopic findings attributed to the administration of the test item consisted of whitening of incisors in main test animals and occasionally broken and/or lost incisors after the recovery period (Fig. 17). Along with this symptoms, the body-weight gain in high dose males was moderately lower compared to controls, slightly lower in the mid dose males, although the food intake in males was not very different between treated and control animals.

Histopathologically, lesions in teeth consisted of focal/ multifocal necrosis or apoptosis and/or degenerative shrinkage of odontoblasts up to a complete loss of odontoblasts along with the formation of dentin niches and thinning of dentin layers (Fig. 18). In the latter cases, the inner lumen of the pulp was irregular and the dentin was basophilic discoloured whereby the discoloration was mainly due to the formation of basophilic granulations within the dentin (Fig. 19). Aberrant dentin-like material was recorded within the pulp cavity but also within the root sheaths. Furthermore, degeneration and/or disorganisation of ameloblast layers up to a complete loss of these cells was noted. The degenerative changes led to clumping of ameloblast remnants and loss of enamel (Fig. 20). Rarely, there were residua of enamel within cyst-like structures (Fig. 21). In the latter cases, the dental epithelial sheath was moderately atrophic characterized by thinning of connective tissue (Fig. 22). In single cases, the pulp mesenchymal was replaced by fibrosis and inflammatory infiltrates. Similar findings were observed after the recovery period, i.e. these tissues did not recover.
Neoplasms in rats, mice and dogs

Amongst the lesions of control WistarHan: RCC rats collected at RCC Ltd in more than 40 oncogenicity studies, there was only one case of a compound odontoma (Fig. 23). This tumor was highly differentiated consisting of numerous denticles within the tumor mass. These denticles showed all tissues of a normal tooth including dentinum, cementum and enamelm, pulp-like structures, and layers of odontoblasts and ameloblasts were visible. In test-item treated animals of negative oncogenicity studies, there was one ameloblastoma (Fig. 24) diagnosed that was not related to treatment. This tumor was mainly composed of epithelial islands mimicking the enamelm with central stellate cells resemble those in normal teeth.

In a 26-week dermal study performed with 160 Tg.AC mice, there were 25 odontogenic neoplasms (15.6%). These neoplasms were randomly distributed throughout the groups, whereby 14 (17.5%) were recorded in males and 11 (13.8%) in females. From these neoplasms, the following tumor types were diagnosed: 8 cementing fibromas, 3 compound odontomas, 1 complex odontoma, 9 ameloblastic odontomas, and 4 ameloblastomas. The neoplasms were diagnosed based on classical features, i.e. the complex odontoma (Fig. 25) contained dental pulp mesenchymal cells and hard tissues but was less differentiated as the aforementioned compound odontoma (Fig. 26) and resembled little to normal tooth. The ameloblastic odontomas (Fig. 27) resembled ameloblastoma (Fig. 28) but contained certain amounts of hard tissues including cementum, dentin and/or enamel whereby the soft tissue component usually was located peripherically. The ameloblastic component was considered to behave aggressively. The ameloblastomas did not form hard tissues or stroma resembling periodontal ligament. Most tumors showed a plexiform or follicular (epithelial islands mimicking the enamel with central stellate cells resemble those in normal teeth) growth pattern. The cementifying fibroma was considered to originate from the periodontal ligament and was characterized by foci of bone or cementum within a mass of spindle-shaped cells (Fig. 29).

Furthermore, there were 4 cases of chronic active inflammation, 1 case of periodontal ligamentum hyperplasia leading to a uniform thickening of the ligament (Fig. 30), and 4 cases of dental dysplasia.

The author is unaware of any spontaneous odontogenic tumor in laboratory beagle dogs. Odontogenic tumors are in general rare in dogs too. As an example, a typical spontaneous case of an ameloblastic odontoma (Fig. 31) from a Cruce Husky female dog at 4 months in age was provided by Dr. Jordi Alumá (AnaPath GmbH, Switzerland). The neoplastic tissues were characterized by the features described above.

Discussion

Regarding tooth lesions in rodents, it should be considered that the initial step of any tooth lesion would not be recorded at the end of a regular toxicity study. This is due to the high rate of growth of the rat’s incisors (the adult rat’s upper incisors grow on average about 2.2 mm per week or 0.31–0.32 mm per day), and the lower incisors grow about 2.8 mm per week (0.4 mm per day). It takes about 40–50 days for new tooth for the generation from the base to reach the tip. The entire tooth is therefore never more than 40–50 days old. Due to the high growth rate and renewal time for teeth as described above, the monophyodont (one set of teeth) rodent incisor cannot be directly compared with human teeth. Rodent incisors are hypsodont (complex teeth), i.e. the formative organ is persisting life-long. Therefore, it must be considered that after the renewal time (40–50 days in rats) the target cell cannot be established anymore as mentioned before. Mechanistic studies may be performed to detect the initial lesions. The final stage of any tooth lesion will result either in dental dysplasia or the loss of teeth.

In laboratory animals tooth lesions may be either by trauma, acquired or iatrogen in nature, or a consequence by treatment with the test item. Odontogenic neoplasia may be also induced by treatment with a test item or is recorded as spontaneous lesions (Fig. 1).

Examples for acquired alteration in teeth were found in an oncogenicity (inhalation) study performed with CD-1 mice at an age of 4 to 5 weeks at study start. They were small and the inhalation tubes had to be adjusted. A metal bar was used to close the tube on its connection side to the inhalation tower. Mice behaved aggressively biting into this metal. Tooth trauma was a consequence leading to a range of inflammatory lesions including acute to chronic periodontitis along with or without necrosis of the ventral meatus in nasal cavity level 1 (according to Young), intranasal inflammatory exudation, tooth fractures, acute necrotizing pulpitis and related inflammatory processes in the neighboring nasal cavities. Often, a more chronic lesion was along with dental dysplasia. There was no relationship to treatment with the test item. Moreover, approx. 2 months after study start, the metal bar was removed, mice adapted to the administration condition and no further case was recognized. All findings recorded were due to trauma and
Fig. 2. Mouse. Incisor: vascular dilation in pulp cavity with irregular dentin formation, loss of odontoblasts, dentin niches and formation of bone-like structure within pulp (Adquired trauma). HE, lens ×4.

Fig. 3. Mouse. Incisor: vascular dilation in pulp cavity, partial loss of odontoblasts and accompanied by the formation of dentin niches (Adquired trauma). HE, lens ×10.

Fig. 4. Mouse. Incisor: thickening of dentin due to apposition of immature basophilic dentin. Note: odontoblasts are still present. (Adquired trauma). HE, lens ×10.

Fig. 5. Mouse. Incisor: chronic inflammation of pulp and root (Adquired trauma). HE, lens ×20.

Fig. 6. Mouse. Incisor: fragment of fractured tooth partially replaced by mesenchymal tissues. (Adquired trauma). HE, lens ×40.

Fig. 7. Mouse. Incisor: abscess formation in apical pulp (Adquired trauma). HE, lens ×20.
Fig. 8. Mouse. Incisor: acute to subacute inflammation of the adjacent nasal cavity due mechanical injury of nasal bone by tooth fracture (Adquired trauma). HE, lens ×4.

Fig. 9. Mouse. Incisor: dentin dysplasia as result of healing process (Adquired trauma). HE, lens ×4.

Fig. 10. Dog. Molar: chronic granulomatous inflammation in pulp of tooth treated with a positive control in pulp-dentin test. Similar to lesions due to drilling procedure (overheating) during cavity preparation (iatrogenic trauma). HE, lens ×10.

Fig. 11. Rat. Incisor: pulp congestion along with thrombosis, complete loss of odontoblasts and thinning of dentin layers (Test item induced: vasotonus affecting compound). HE, lens ×20.

Fig. 12. Rat. Incisor: partial loss of odontoblasts and formation of dentin niches. Note: osteodentin is present (upper right). (Test item induced: vasotonus affecting compound). HE, lens ×40.

Fig. 13. Rat. Incisor: complete loss of odontoblasts and formation of dentin niches, thrombosis in pulp, and thickening of dentin due to apposition of a more basophilic dentin. (Test item induced: vasotonus affecting compound). HE, lens ×10.
Fig. 14. Rat. Incisor: aberrant dentin (denticles) within the pulp cavity. (Test item induced: vasotonus affecting compound). HE, lens ×20.

Fig. 15. Rat. Incisor: thinning of dentin and partial replacement of thrombus within pulp by bone-like material (osteodentin) (Test item induced: vasotonus affecting compound). HE, lens ×20.

Fig. 16. Rat. Incisor: rarefaction of ameloblasts (Test item induced: vasotonus affecting compound). HE, lens ×40.

Fig. 17. Rat. Incisor: white discoloration. (Test item induced: fluorosis).

Fig. 18. Rat. Incisor: complete loss of odontoblasts and formation of dentin niches with irregular luminal surface and basophilic appearance of dentin. Note: moderate edema within pulp. (Test item induced: fluorosis). HE, lens ×40.

Fig. 19. Rat. Incisor: partial loss of odontoblasts and formation of dentin niches leading to irregular pulp surface. Note: formation of basophilic granulations within the dentin due to resorption. (Test item induced: fluorosis). HE, lens ×40.
Fig. 20. Rat. Incisor: degeneration and/or disorganisation of ameloblast layers up to a complete loss of these and clumping of ameloblast remnants. (Test item induced: fluorosis). HE, lens ×40.

Fig. 21. Rat. Incisor: residua of enamel within cyst-like structures. (Test item induced: fluorosis). HE, lens ×40.

Fig. 22. Rat. Incisor: moderately atrophic dental epithelial sheath characterized by thinning of connective tissue. (Test item induced: fluorosis). HE, lens ×40.

Fig. 23. Rat (WistarHan: RCC, control animal): compound odontoma. Highly differentiated tumor consisting of numerous denticles within the tumor mass. HE, lens ×20.

Fig. 24. Rat (WistarHan: RCC, dosed animal, spontaneous tumor): ameloblastoma composed of epithelial islands mimicking the enamelum with central stellate cells. HE, lens ×20.

Fig. 25. Mouse (Tg.AC): complex odontoma containing dental pulp mesenchymal cells and hard tissues but is less differentiated as compound odontoma. HE, lens ×10.
Fig. 26. Mouse (Tg.AC): compound odontoma. HE, lens ×10.

Fig. 27. Mouse (Tg.AC): ameloblastic odontoma resembling ameloblastoma but also hard as cementum, dentin and/or enamel. The soft tissue component is usually located in the periphery. HE, lens ×10.

Fig. 28. Mouse (Tg.AC): ameloblastoma do not form hard tissues or stroma resembling periodontal ligament. Consisting of a plexiform or follicular (epithelial islands mimicking the enamenum with central stellate cells resemble those in normal teeth) growth pattern. HE, lens ×20.

Fig. 29. Mouse (Tg.AC): cementifying fibroma characterized by foci of bone or cementum within a mass of spindle-shaped cells. HE, lens ×20.

Fig. 30. Mouse (Tg.AC): periodontal ligamentum hyperplasia considered to be prenplastic lesion. HE, lens ×20.

Fig. 31. Dog (female Cruce Husky, 4 months in age): ameloblastic odontoma. HE, lens ×20.
related poor condition. A similar phenomenon in chronic inhalation studies was described following repeated clipping of incisors in rodents due to feeding a powdered diet, which reduced the normal wearing of incisors\textsuperscript{14}. In this report, deformations due to tooth pulp and periodontal abscesses, fractured and necrotic teeth as well as periodontal cysts of the maxillary incisors, diagnosed as dental dysplasia at incidences of 3\% (females) to 9\% (males) of CD-1 mice and 14.5\% (females) to 10.5\% (males) of CD (Sprague-Dawley) rats were reported. Trauma-related repair mechanism as described from the mouse inhalation study above is irrelevant for adult human. Moreover, such case is not influencing the establishment of NOEL or NOAEL. However, the lesion must be considered and should not be misinterpreted as primary toxic effect.

In beagle dogs used for a pulp-dentin test, inflammatory changes in the pulp of teeth treated with a positive control as silicate cement are expected due to the formation of an acid. In negative control, however, and test item-treated teeth, inflammatory reactions may be due to focal overheating by cavity preparation (drilling). The latter was also deemed to be the reason for inflammatory processes regarded in negative control teeth observed in the study described above, and, hence are an example of iatrogenic alterations.

Although rare, test item-related lesions in tooth need to be considered for unknown products. An example for such induced lesions was found under treatment with a compound acting on the vasotonus consisting of degeneration of odontoblasts and/or ameloblasts, pulp degeneration characterized by angiectasis, congestion, thrombosis, necrosis and/or fibrosis and dentin hypertrophy or atrophy and/or dentin dysplasia. The mechanism leading to the above described lesions is considered due to vascular dilation in pulp tissues, mechanical trauma of odontoblasts and following repair mechanism in form of dental dysplasia.

To the knowledge of the author, similar lesions are not published on other compound acting on the vasotonus as there are endothelin antagonists, e.g. bosentan. Moreover, in a publication about adverse effects in humans due to bosentan, the incidence of toothache was even lower in the treated groups than in the placebo group\textsuperscript{15}.

Another interesting example of test item-induced lesions was recorded under treatment with a fluorinated compound in a 28-Day (gavage) study in Sprague Dawley rats. The most remarkable gross lesion were recorded as whitened or bleached incisors during the main test. During the recovery period, the finding persisted and there were even cases where incisors broke or were lost. The histopathological correlate consisted of focal to multifocal necrosis and/or degeneration of odontoblasts up to a complete loss of these cells along with degeneration (thinning, change in coloration, formation of dentin niches) of the dentin and in single cases of dysplastic foci of dentin. Also, the epithelial sheath of the roots degenerated, indicated by thinning and loss of collagen and cellular components. The ameloblasts became disorganized, expressed degeneration by shrinking or were necrotic or completely lost leading to the loss of enamel. In single cases, there were foci of aberrant enamel within niches formed by the remaining connective tissue of the epithelial sheath. The pulp lumen was widened in most cases due to loss of dentin thickness. The dentin niches led to a rough inner surface. Edema, necrosis and pulpititis were often recorded. Similar findings were observed after the recovery period, i.e. these tissues did not recover. A similar lesion as observed in the present study may be produced by increased fluoride uptake in human whereby mainly children are affected during the amelogenesis period\textsuperscript{16}. With increasing severity of fluorosis, the subsurface enamel all along the tooth becomes increasingly porous (hypomineralized), and the lesion extends toward the inner enamel. In dentin, hypomineralization results in an enhancement of the incremental lines. After eruption, the more severe forms are subject to extensive mechanical breakdown of the surface\textsuperscript{17}.

In animal models it was demonstrated that G proteins participate in the disturbance of intracellular transport of the secretory ameloblast exposed to fluoride\textsuperscript{18}. The NTP (1990) performed toxicology and carcinogenesis studies with sodium fluoride in drinking water in F344/N rats and B6C3F1 mice. Sodium fluoride is a white, crystalline, water-soluble powder used in municipal water fluoridation systems, in various dental products, and in a variety of industrial applications. In 6-months studies, the teeth of rats and mice receiving the higher doses of sodium fluoride were chalky white and chipped or showed unusual wear patterns. Mice and male rats given the higher concentrations had microscopic focal degeneration of the enamel organ. In carcinogenicity studies, the teeth of rats and mice has a dose-dependent whitish discoloration, and in male rats a higher incidence of tooth deformities and attrition leading on occasion to malocclusion were recorded. The teeth of male and, to a lesser degree, female rats had areas of microscopic dentine dysplasia and degeneration of ameloblasts. Dentine dysplasia occurred in both dosed and control groups of male and female mice; the incidence of this lesion was significantly greater in high-dose than in control male mice. Neoplasms however were not reported\textsuperscript{19}. Although, the mechanism of the lesions in the herewith presented study could not be established, a multiple target including both, odontoblasts and ameloblasts may be considered. A mechanism similar to that described for fluoride is likely.

Generally, tooth lesions recorded in toxicity studies are warning signals for all new products when treating non-adults. From the fluorinated compound-produced lesions it cannot be predicted if similar lesions may be recorded in future by use of this medication. However, similar lesions due to high uptake of fluoride in childhood are described as fluorosis in humans\textsuperscript{20}, and hence may be relevant for human.

Neoplasia may be recorded laboratory animals either induced by chemical products, or intrinsic as background lesion due to genetical predisposition. Odontogenic tumors are rarely encountered as spontaneous lesions in rats (presented in table 1) but may be induced by carcinogens e.g. M-ethyl-N-nitrosourea\textsuperscript{21}, methylnitrosourea\textsuperscript{22}, aflatoxins\textsuperscript{23}, methylnitrosourea \textsuperscript{22}, aflatoxins\textsuperscript{23},
or are rare genetically induced lesions as in op/op rats. In Table 1, an overview on published odontogenic tumors is presented.

In mice, spontaneous odontogenic tumors are even rarer. To the authors knowledge, there are only two cases known, a complex odontoma in a Swiss (CD-1) mouse and ameloblastic fibro-odontoma in mouse. In contrast, in homozygous transgenic mice (TG.AC), the 1-year incidence of odontogenic tumour formation in these mice was approx. 35%. Tg.AC transgenic mice, a mouse line created in the FVB/N mouse strain by pronuclear injection of v-Ha-ras oncogene, provide a sensitive alternative to the two stage initiation/promotion model oncogenic agents, especially as a model of skin tumorigenesis. The oncogene is fused at the ζ-end to a foetal ζ-globin promoter and linked at the 3’-end to a SV-40 polyadenylation/splice sequence. The transgene is transcriptionally silent until activated by wounding, UV light or exposure to promotors. Therefore, the incidence of odontogenic tumors at 15.6% as recorded in the 26-week study presented above, is not unusual. Interestingly, although odontomas are not considered to be true neoplasms but redundancies of the dental organ secondary to malocclusion and/or injury and proliferation of the dental organ, this is deemed to be unlikely regarding the proportion of different types of odontoma (compound, complex, ameloblastic) diagnosed in this study. Precursors of neoplasia in the presented study were considered to be inflammatory processes or in one case periodontal ligament hyperplasia.

As in rats and mice, odontogenic tumors are rarely encountered in dogs without preference in breed and sex. However, the author is unaware of any spontaneous odontogenic tumor in laboratory beagle dogs.

### References


