From: The Department of Oral Pathology, The Royal Dental College, Copenhagen.

PERIODONTAL TISSUE CHANGES INDUCED IN YOUNG RATS BY ROENTGEN IRRADIATION OF THE MOLAR REGIONS OR THE HEAD

by

ASGER M. FRANDSEN

Observations made on humans as well as experimental animals indicate an adverse effect of ionizing radiation on the periodontal tissues. In humans, radiation-induced periodontal pathology has primarily been studied in patients treated for malignant tumors of the oral and adjacent regions by external or internal irradiation. The main interest has been focused upon the role of periodontal disease as a possible portal of entry for infection in the development of radio-osteomyelitis. Ulceration of the gingiva, bleeding and suppuration, denudation of roots and bone, stomatitis, and progressive periodontitis with loosening and loss of teeth are the changes described (*Ellinger* 1957, *Gotthard* 1923, *Leist* 1927, *Regaud* 1922, *Stafne* 1947). Resorption of alveolar bone and teeth, as revealed by roentgenograms, was found to be a late effect of internally deposited radioactive materials (*Aub, Evans, Hempelmann, & Martland* 1952). These authors further stated that coarsening of the trabeculation of the alveolar crest was a consistent finding, but they did not consider it diagnostic of radiation damage. On the whole, the evaluation of these observations, mainly obtained from elderly patients,

This investigation was supported by a grant from the Danish State Research Foundation.

suffers from the insufficiency inherent in not knowing the pre-irradiation state of the periodontal tissues, and from the lack of uniformity inevitably associated with human material.

Further clarification of the effects of irradiation on the periodontal tissues has been attempted by animal experimentation employing monkeys, dogs, rabbits, mice, and rats. *Medak & Burnett* (1954), working with the Macacus rhesus monkey, exposed the heads of young animals to fractionated doses of roentgen rays ranging from 4,200 r to 6,000 r. The resulting periodontal changes were necrosis of the gingiva with eventual sloughing and exposure of underlying necrotic alveolar bone. Roentgenographically, reduced height of the alveolar crest and widening of the periodontal space were demonstrated. In the higher dose ranges, loss of most of the bony support of the molars caused loosening of these teeth. *Gowgiel* (1960) irradiated the jaws of young Macacus rhesus monkeys with 4,500 r to 11,000 r given as fractionated doses of roentgen rays. He observed necrosis of the gingiva, destruction of the periodontal ligament, and resorption of the alveolar bone. Changes of the arterioles resembling arteriolosclerosis were also noted. It was pointed out that the interdental papillae were the first tissues to be affected in all the animals examined.

Leist (1926) produced loosening and loss of single teeth by irradiating the jaws of young dogs with 8 to 10 Holzknecht units of roentgen radiation. In a subsequent study (*Leist* 1927), the doses were increased to 30 H to 45 H. The microscopic changes observed were a diminished number of principal periodontal fibres and an edematous fibrous bone marrow with reduced vascularity. *Zerosi* (1938, 1940) irradiated the maxillary molar regions of young dogs, either with 800 r to 900 r of roentgen rays, or by implantation of radium in the same regions. Two to three weeks after the irradiation the animals exhibited gingival changes consisting of albuminous degeneration, coagulation necrosis, and degeneration of collagen fibres. In the periodontal membrane similar degenerative changes in connection with hyperemia, exudation, and reduced cellularity were noted. The alveolar bone displayed resorption and fibrous transformation of the marrow. The initial effect on the periodontal tissues was considered to be an effect on the vessels resulting in thrombosis

and in degeneration of the walls of the vessels. *English, Wheatcroft, Lyon, & Miller* (1955), also studying dogs, irradiated the heads with single doses of 1,000 r to 1,750 r roentgen rays. They observed changes ranging from mild gingivitis to sloughing of the gingival and buccal mucosa. The irradiation of the mandible of dogs with fractionated doses amounting from 3,000 r to 8,000 r (*Chambers, Ng, Ogden, Coggs, & Crane* 1958; *Ng, Chambers, Ogden, Coggs, & Crane* 1959) caused a pseudo-membranous mucositis and edema of the gingiva. Later, in the animals which received the higher doses, exfoliation of teeth occurred. The microscopic changes consisted of replacement of the epithelial attachment by a fibrino-purulent exudate and the extending of pronounced inflammatory changes into the alveolar bone and the periodontal membrane.

Young rabbits, which were given radium sulphate *per os* (*Rosenthal* 1937), exhibited resorption of the roots and ankylosis. In the periodontal membrane, extreme hyperplasia of the fibroblastic tissue and development of cysts from the epithelial remnants were described.

The effects of ionizing radiation on the oral tissues of newborn mice were investigated by *Burstone*. The sources of the irradiation were P^{32} injected subcutaneously (1950 a) or adjacent to the mandible (1951), radioactive colloidal gold injected adjacent to the mandible (1950 c), and 50 KV-roentgen rays given in doses varying from 1,500 r to 5,000 r to the molar and mandibular joint areas (1950 b). The effects on the periodontal tissues were disturbed osteogenesis and marrow aplasia of the alveolar bone, cellular infiltration and necrosis of the interdental papilla and the periodontal membrane, and ankylosis. *Greulich & Ershoff* (1961) exposed young mice to six weekly doses of 200 r total body roentgen irradiation. After a latent period of several months the periodontal changes were first manifested as lesions of the sulcus lingually and mesially to the first molars. Then followed involvement of the other molars with deepening of the gingival sulcus, invasion by a bacterial plaque, and eventual exfoliation of the teeth. The histologic findings were degeneration of connective tissue and alveolar bone, lytic changes of the collagen bundles associated with the presence of inflammatory cells and necrosis, and necrosis and resorption of the cementum. There

was a minimal response of the gingival epithelium to the bacterial plaque. The lesions were predominantly observed in mice on a purified diet, whereas others, maintained on a stock diet, exhibited little evidence of pathologic alterations.

Dale (1953, 1957) exposed young and older rats to single doses of total body roentgen irradiation ranging from 375 r to 750 r in order to study the effects on the incisor tooth. No detailed histologic study of the periodontal tissues was carried out, but gross changes consisting of edema and bleeding of the gingiva, and petechiae and ulcerations of the oral mucosa were noted. Other rats were exposed to chronic total body roentgen irradiation consisting of 75 to 90 daily doses of 10 r to 20 r with or without a terminal dose of 600 r. These animals displayed widening of the periodontal membrane, and disrupted and inhibited deposition of secondary cementum. *Fedorov & Prokhonchukov* (1959) exposed two month old rats to fractionated roentgen ray doses totaling 300 r to 3,500 r and examined the changes manifested after five to six months. Severe oral changes were observed in the rats receiving more than 2,000 r, consisting of necrosis and atrophy of the gingiva, a necrotic stomatitis, development of pusfilled pathologic pockets, and resorption of alveolar bone leading to denudation of the roots and loosening of the teeth. Sequestration and pathologic fracture of the jaw bone were also noted. No histologic data were reported.

From this review of the literature it appears that no detailed histologic study of the periodontal changes in the rat subsequent to local roentgen irradiation has been carried out. In a previous report (*Frandsen* 1962), radio-osteomyelitis of the jaws was produced in rats by local roentgen irradiation, preceeded or followed by tooth extraction. In the light of the prevalent clinical impression that periodontal disease in irradiated jaw areas may be a portal of entry for infection leading to radio-osteomyelitis, it was considered of interest to study the periodontal tissues of the author's rat material.

Thus, the purposes of the present study were the following:

1) To supplement experimental data on the histologic changes produced in the rat periodontium by local roentgen irradiation.

2) To relate the pathologic changes of the periodontium to the development of radio-osteomyelitis.

MATERIAL AND METHODS

Two main groups of male Wistar rats were available. The first group consisted of 37 rats which were divided into two subgroups of 27 and 10. At the ages of 56 ± 4 days these rats were irradiated on the molar regions with 1,725 r and 2,400 r respectively, given as single doses of roentgen rays. The second group comprised 21 rats which were divided into three subgroups of 7 and, at the same ages, irradiated on the heads with single roentgen doses of 1,000 r, 2,000 r, and 3,000 r respectively. In addition, the first group contained 21 unirradiated control rats, the second group nine controls. The rats were killed at various intervals after the irradiation ranging from 2 to 58 days. The diet consisted of a hard and coarse stock ration.

The physical factors of irradiation were: 200 KV, 20 Ma, filters: 0.5 mm Cu and conic Al (1—7×0.32 mm). The upper and lower right molars were sectioned serially in a mesio-distal direction, and stained with hematoxylin and eosin and Van Gieson's connective tissue stain. A detailed description of the experimental technique may be found in a previous report (*Frandsen* 1962).

RESULTS

With regard to the gross pathologic changes, reference is made to the above-mentioned report. The histologic findings from the two main groups will be described separately. The evaluation of these findings must necessarily rest upon a concept of the normal condition. Some of the reports describing pathologic changes of the rat periodontium presumably caused by certain experimental conditions seem to indicate deficiencies in familiarity with the range of behavior normally exhibited by these tissues. Rather than representing a well defined, singular status, the periodontium of the control rats may exhibit a variety of changes, which must be considered in the evaluation of the cause —effect relationship. The following examination of the control material stresses features relevant to the present study.

Periodontal tissues of the control rats

In Plate 1 are illustrated various degrees of inflammatory changes of the periodontal tissues in control rats. An almost ideal

condition of the interdental papilla is seen in Fig. A. The epithelial covering consists of a few layers of cells, and the connective tissue exhibits a minimum of inflammatory cells. Only a small area of epithelial proliferation is noted. A resting group of epithelial remnants may be seen in the periodontal membrane. In Fig. B the interdental papilla consists mainly of proliferating epithelial cells with interspersed edema and inflammatory cells. A small area of round cell infiltration is noted in the subepithelial tissue. A further step in the involvement of the periodontium is illustrated in Fig. C, where the round cell infiltration is more extensive, and lysis of some of the transseptal fibres is evident.

Epithelial proliferation as a reaction to the impaction of foreign bodies may appear in various ways in histologic sections. In Fig. D, there is continuity between the surface epithelium and the deeper, proliferating cells, whereas in Fig. E, the proliferating epithelial cells appear as "islands" in the periodontal membrane. In such instances, serial sectioning will frequently reveal a connection with the surface layer. A periodontal abscess situated deeply in the interdental tissues is illustrated in Fig. F. In this case serial sectioning disclosed foreign body impaction as the causative agent.

On the whole it may be stated that the control material exhibited varying degrees of inflammatory changes of the interdental tissues. Epithelial proliferation in connection with interspersion of edema and inflammatory cells were frequent findings. Apparently, the proliferating cells were those lining the interdental papillae, whereas those adjacent to the cementoenamel junction displayed the least activity. Thus, in the absence of foreign body impaction, there was no evidence of pocket formation. In connection with the epithelial changes, the subepithelial connective tissue displayed some degree of round cell infiltration and lysis of the principal fibres. The majority of the control rats exhibited changes in the range illustrated by Figs. B and C, whereas the conditions illustrated in Figs. A and F were exceptional.

Other variations within the control material are illustrated in Plate 2. The size of the marrow cavities of the alveolar bone has been used as an indication of pathologic changes. However, if the

anatomy of the rat molars is considered (*Sicher & Weinmann* 1944), it is realized that the plane of sectioning determines the bone—marrow relationship. Figs. A and B represent two sections from the same specimen, a lower first molar. Fig. A shows a central section with a large marrow cavity, whereas, more buccally, the alveolar bone of the accessory root was sectioned tangentially and thus gives the impression that only a little marrow tissue is present (Fig. B). Likewise, the height of the interdental septum as judged by the distance from the crest to the cemento-enamel junction is subject to misinterpretation. Firstly because any deviation of the plane of sectioning from the long axis of the teeth will distort this relationship, and secondly because the crest does not normally constitute a straight line bucco-lingually. The same septum will consequently exhibit varying heights in serial sections.

More significant information about the state of the alveolar bone may be obtained from an estimation of the relation between bone destruction and bone formation, and of the amount of bone serving as insertion for the periodontal fibres. In considering bone resorption versus bone apposition, the normal distal drifting of the rat molars must be taken into account. This means that bone resorption will usually prevail on the alveolar surfaces facing mesially, and bone formation on those facing distally (Figs. C and D). Resorption of the cementum of the distal root surfaces may accompany this process. Figs. C and D further illustrate the influence of the distal shifting on the periodontal membrane. Where bone and cementum are being resorbed, there is no orderly arrangement of the cells and fibres, whereas on the apposition side, there is a distinct orientation of these elements.

The marrow tissue of the control animals in the present age range is hematopoietic (Figs. A and B), and the histologic technique used results in osteocytes with an appearance illustrated by Figs. C and D.

Periodontal tissues of the irradiated rats

A. Irradiation restricted to the molar regions

The two groups of rats receiving 1,725 r and 2,400 r respectively on the molar regions displayed minor quantitative but no

qualitative differences of the pathologic changes. Therefore, they will be described as one group.

It was a significant finding that the more severe periodontal changes did not originate as such, but were secondary to ulcerations of the oral mucous membrane initiated elsewhere. Fig. A in Plate 3 illustrates a small ulceration situated anterior to a lower first molar of a 69 day old rat killed 12 days after irradiation with 2,400 r. The ulcerated area is covered by pus and there is moderate round cell infiltration of the subepithelial tissue. A pronounced edema of the submucosa is noted. Another ulceration is situated on the lower border of the tongue, and there is an accumulation of pus at the gingival margin mesial to the first molar. The interradicular septum of this tooth is being resorbed by numerous osteoclasts and the hematopoietic marrow replaced by fibrous tissue. No changes of the tissues between the first and second molars are noted.

An aggravation of this condition is seen in Fig. B from a 100 day old rat killed 48 days after irradiation with 1,725 r. Ulceration and necrosis have extended in width and depth to involve the entire area anterior to and around the first molar. The interradicular area of this tooth is also affected. Pus formation and extensive bone resorption are noted. The periodontal tissues distal to the first molar only exhibit minor morphologic changes.

Fig. C illustrates a case in which the initial soft tissue lesion is posterior to the third molar. This rat, killed when 104 days old and 47 days after irradiation with 2,400 r, developed an extensive necrotic lesion causing destruction and sequestration of a portion of the mandible and incisor tooth. The periodontal tissues of the third molar are destroyed to the extent that the tooth is practically exfoliated. The roots and the sequestra are covered by bacterial masses. Apart from the area between the third and second molars, the remaining periodontal tissues are but little affected.

The changes located to and originating in the periodontal tissues were less conspicuous but still significant (Plate 4). The epithelial proliferation normally associated with lesions of the interdental papilla was suppressed or absent. Fig. A illustrates this condition in a rat killed at the age of 100 days, 48 days after the irradiation. Despite the lack of a sufficient epithe-

lial covering, there is only little round cell infiltration in the subepithelial tissue. This suppression of cellular activity is also manifested elsewhere. Fig. B illustrates the interdental septum of a 65 day old rat, 13 days after the irradiation. It is noted that the resorption—apposition pattern is absent, indicating a "passive" septum. A pseudomembraneous covering of the oral mucosa was a frequent macroscopic finding at the autopsy of the irradiated animals. Fig. C illustrates the gingiva mesial to the first molar of a 69 day old rat, 12 days after the irradiation. A plaque is seen anterior to the gingival margin, and the submucosa of this area exhibits pronounced edema. The condition of the gingival and periodontal fibres was also examined by staining for collagen. The gingival margin mesial to the first molar of a 69 day old rat, 12 days after the irradiation, is illustrated in Fig. D. The ordinary appearance of the fibres is here replaced by an amorphous clumping of the collagen. Other changes included endothelial cell proliferation as described earlier (*Frandsen* 1962), and hyperemia of the bone marrow and the periodontal membrane.

B. *Irradiation of the entire head*

The group of rats given 1,000 r to the head displayed no serious effects of the irradiation during the observation period. The rats killed at the termination of the experiment, 151 days old and 93 days after the irradiation, appeared healthy and were still growing. Histologically, the oral mucous membranes and the gingivae of these rats exhibited no deviations from the same tissues of the control animals. Thus, the interdental papillae displayed proliferation of the epithelium and round cell infiltration as a reaction to foreign body impaction (Plate 5, Fig. A). However, changes of the deeper periodontal tissues could be observed. In Fig. A it is noted that the supra-alveolar connective tissue is poor in cells, and that the osteocytes of the interdental septum display pyknotic hyperchromatic nuclei. Further, the apposition—resorption pattern is absent. Fig. B illustrates similar changes of the osteocytes of the intraradicular alveolar bone of a 96 day old rat, 38 days after the irradiation. The hematopoietic marrow is apparently intact.

The rats irradiated with 2,000 r and 3,000 r on the head all became moribund within 8 to 10 days and died or were killed in a state of extreme emaciation and dehydration. The oral changes were similar in all the irradiated animals. The epithelium of the mucous membrane became necrotic and sloughed off leaving the underlying tissue denuded or covered by a layer of fibrinous exudate and pus. The gingival margin mesial to the first molar of a rat, killed 9 days after the irradiation, is illustrated in Fig. C. The epithelium of the gingival margin is seen, but that of the adjacent mucous membrane has disappeared and is replaced by an accumulation of pus cells. In other rats of these groups, the gingival epithelium was destroyed as well. The interdental papillae were frequently completely denuded of epithelium, and the connective tissue core displayed a deficient inflammatory reaction. In Fig. D, 8 days after the irradiation, is illustrated an interdental papilla in which the cellular reaction is virtually absent.

DISCUSSION

Because of the minor changes caused by 1,000 r, and the lethal effect produced after 8 to 10 days by 2,000 r and 3,000 r, administered to the entire head, the present study was not well suited for a comparison between the periodontal changes caused by head and jaw irradiation. The degenerative changes of the alveolar bone and the periodontal membrane observed in the 1,000 r group suggest that more severe pathologic changes could have been observed, had the animals been subjected to longer observation periods. The almost uniform "burning away" of the epithelial lining of the oral mucous membrane observed in the 2,000 r and 3,000 r groups is comparable to the loss of epithelial lining of the intestines of animals given total body irradiation, and succumbing to "intestinal radiation death". The loss of oral epithelium may be an important factor in the syndrome leading to "oral radiation death" (*Quastler, Austin, & Miller* 1956).

The rats irradiated only on the molar regions with 1,725 r and 2,400 r developed a variety of periodontal lesions and no lethality interfered with the preplanned observation periods. It

was a significant finding, that when serious periodontal lesions did develop, they were always seen in connection with ulcerations of mucous membrane areas closely related to, but not part of the periodontal tissues (Plate 3). Further, it was characteristic that the periodontal tissues closest to the mucous membrane lesion were the most affected whereas the remainder were conspicuously unaffected. Finally, severe periodontal lesions were not observed in rats which did not display lesions of the adjacent mucous membrane areas. Consequently it may be stated that the severe periodontal destructions observed in some of the rats, did not originate as lesions of the periodontium, but were secondary to ulcerations of the adjacent mucous membrane. The infectious processes thus established could expand relatively unopposed in the radiation-damaged tissue. This mode of development of the severe periodontal lesions in the present rat material was in contrast to observations made on monkeys (*Gowgiel* 1960) and dogs (*Chambers et al.* 1958; *Ng et al.* 1959) in which the destruction of the periodontium was initiated in the gingiva.

Lesions of the type discussed above and illustrated in Plate 3 were not frequent. The majority of the rats displayed changes of the category illustrated in Plate 4. They were mainly manifestations of suppression of cellular activity and they could be demonstrated by (1) lack of epithelial cell proliferation as a reaction to foreign body impaction, (2) a deficient inflammatory reaction, and (3) absence of the apposition—resorption activity normally seen at the alveolar septa. Further, changes of the collagenous fibres were noted.

No direct comparison can be made between the results of the present study and others relating radiation-induced periodontal changes in rats as the experimental conditions vary, and because the previous studies (*Dale* 1953, 1957; *Fedorov & Prokhonchukov* 1959) include no detailed histologic descriptions. However, it is apparent that ulceration and necrosis of the oral mucous membrane occurring separately or in association with periodontal lesions were findings in all the experiments. In mice (*Greulich & Ershoff* 1961) the initial oral lesion frequently appeared at the mesio-lingual aspects of the first molars and at the disto-lingual aspect of the third molars. Further, involvement of single teeth was noted. Although these changes were found in mice receiving

fractionated doses of total body roentgen irradiation, they are strikingly similar to some of the changes observed in the present study and illustrated in Plate 3.

With regard to other animal species, it is of interest that *Gowgiel* (1960) in his monkey material constantly found the periodontal changes to be initiated by lesions of the interdental papillae. From this region, the necrosis extended to the periodontal tissues and to the oral mucous membrane as well.

In dogs, changes of the epithelial lining of the oral mucous membrane were also characteristic of radiation damage (*Chambers et al.* 1958; *English et al.* 1955; *Ng et al.* 1959; *Zerosi* 1938, 1940). From the surface lesion, inflammatory, degenerative, or necrotic processes extended into the deeper periodontal tissues. In the bone marrow, edema and fibrous transformation were salient features.

In all animal species loss or loosening of teeth was caused by inflammatory changes superimposed on decreased resistance to infection, and leading to destruction of the principal fibres and resorption of the alveolar bone.

The rats used in the present study were subjected to extraction of a molar resulting in the development of radio-osteomyelitis in certain of the irradiated animals (*Frandsen* 1962). This condition was characterized by a penetrating destruction of the jaw of an infectious nature with extensive soft and hard tissue necrosis associated with resorption and sequestration of bone. The process originated in the socket area and extended to the adjacent regions. The study of the periodontal changes in jaw quadrants where no extractions had been performed revealed no instances of the development of radio-osteomyelitis from pathologic processes initiated in the periodontal tissues proper. Whenever radio-osteomyelitis was found in connection with periodontal alterations (Plate 3, Figs. B and C), it was considered to be an extension of an inflammatory necrotizing process initiated by ulcerations of mucous membrane areas adjacent to, but not part of the periodontium.

CONCLUSIONS

Irradiation of the head with 1,000 r did not alter the response of the interdental papillae to local traumata. The occurrence of

epithelial proliferation and round cell infiltration was comparable to that seen in the control animals. A decreased cellular content of the supra-alveolar connective tissue was noted, and the alveolar bone displayed osteocytes with pyknotic hyperchromatic nuclei.

When the doses were increased to 2,000 r and 3,000 r, the rats became moribund within 8 to 10 days. All animals exhibited similar oral changes consisting of an almost complete desquamation of necrotized epithelium.

The changes produced by irradiation of the molar regions with 1,725 r and 2,400 r respectively may be divided into two categories.

The first, representing only a few of the irradiated rats, was characterized by extensive destruction of the periodontium of a single molar leaving that of the other two molars relatively unaffected. These lesions were initiated outside the periodontal tissues.

The second, representing the majority of the rats, was characterized by changes distributed evenly throughout the periodontal tissues of all molars. They consisted of suppression of the epithelial proliferation seen in control rats as a reaction to various local traumata, a deficient cellular inflammatory response, clumping of the collagenous fibres, suppression of osteoclast and osteoblast function, and degenerative changes of the osteocytes.

Both categories of changes were comparable to, but not identical with, other radiation-induced periodontal changes reported in studies of rats and other experimental animals. Some of the discrepancies may be due to variations in the irradiation techniques applied. However, an interesting species difference appears to exist regarding the pathogenesis of the more severe lesions. In monkeys and dogs these lesions appear to originate in the periodontal tissues proper whereas in rats and mice they seem to be preceeded by ulcerations of nearby oral mucous membrane areas.

In the present study, radio-osteomyelitis could not be observed as a direct sequela to periodontal damage. When radio-osteomyelitis was observed in connection with periodontitis, both processes were initiated by mucous membrane ulcerations.

SUMMARY

The periodontal tissue reaction to local roentgen irradiation was studied in two groups of young male Wistar rats. One group was irradiated on the heads with single doses of 1,000 r, 2,000 r, and 3,000 r respectively, whereas the other received single doses of 1,725 r and 2,400 r respectively administered to the molar regions only. The animals were observed over periods ranging from 2 to 58 days after the irradiation.

In the first group, the rats irradiated with 1,000 r displayed a decreased cellularity of the periodontal membrane, degeneration of the osteocytes, and suppressed activity of osteoblasts and osteoclasts. The rats which received 2,000 r and 3,000 r all became moribund or died within 8 to 10 days, exhibiting a characteristic "burning away" of the epithelial lining of the oral cavity.

In the second group, two types of periodontal lesions could be distinguished. One was characterized by severe destruction of the periodontium of either the first or the third molar, leaving the other molars relatively unaffected. These lesions were initiated by ulcerations of adjacent parts of the oral mucous membrane. The other type comprised less severe changes originating in the periodontal tissues proper. They consisted of a lack of proliferation of the interdental papilla epithelium, a deficient inflammatory response, clumping of the collagen, and suppression of the functions of the osteoblasts and osteoclasts.

Radio-osteomyelitis of the jaws was observed, but it was not considered to be a direct sequela to periodontal lesions.

RÉSUMÉ

DES ALTÉRATIONS DES TISSUS PARODONTALES DE JEUNES RATS CONSECUTIVES A L'ACTION DES RAYON X SUR LES REGIONS MOLAIRES OU LA TÊTE

La réaction des tissus parodontales au traitement local par les rayon X fut étudiée chez deux groupes de jeunes rats Wistar. L'un des groupes fut irradié sur les têtes avec des doses singulières de 1,000 r, 2,000 r et 3,000 r respectivement, tandis que l'autre fut irradié exclusivement sur les régions molaires avec 1,725 r et 2,400 r respectivement. Les périodes d'observation allèrent de 2 jusqu'à 58 jours après la radiation.

Les rats du premier groupe irradiés de 1,000 r présentèrent un nombre réduit de cellules du ligament alvéolo-dentaire, une dégénération des ostéocytes et une activité diminuée des ostéoblastes et des ostéoclastes. Les rats irradiés de 2,000 r et 3,000 r furent moribonds ou moururent après 8 a 10 jours, montrant une nécrose et desquamation de l'epithelium buccale.

Dans le deuxième groupe deux types de lésions parodontales se distinguèrent. L'un était caractérisé par une déstruction grave des tissus parodontales soit de la première soit de la troisième molaire, laissant les autres molaires relativement intactes. Ces lésions furent initiées par des ulcérations des parties adjacentes de la membrane muqueuse. L'autre type comporta des altérations moins sévères, qui tirèrent leur origine des tissus parodontales proprement dis. Elles consistaient d'un manque de prolifération de l'épithelium de la papille interdentaire, d'une réaction inflammatoire diminuée, d'une agglomeration du collagène et d'une fonction réduite des ostéoblastes et des ostéoclastes.

Des cas de radio-ostéomyelite des mâchoires furent observés, mais ces affections ne furent pas considérées comme des effets directs des affections parodontales.

ZUSAMMENFASSUNG

PARODONTALE GEWEBSVERÄNDERUNGEN BEI JUNGEN RATTEN ALS FOLGE VON RÖNTGENBESTRAHLUNC DER MOLARREGIONEN ODER DES KOPFES

An zwei Gruppen junger Wistarratten wurde die parodontale Gewebsreaktion nach lokaler Röntgenbestrahlung untersucht. Die eine Gruppe erhielt eine Bestrahlung der Köpfe mit Einzeldosen von je 1,000 r, 2,000 r und 3,000 r, während bei der anderen Gruppe lediglich eine Bestrahlung der Molarregionen mit Einzeldosen von je 1,725 r und 2,400 r vorgenommen wurde. Die Versuchszeit erstreckte sich auf einen Zeitraum von zwischen 2 und 58 Tagen nach der Bestrahlung.

In der ersten Gruppe wiesen die Ratten, die mit 1,000 r bestrahlt worden waren, in ihrer Wurzelhaut einen herabgesetzten Zellgehalt auf, ferner lag eine Degeneration der Osteozyten und eine herabgesetzte Tätigkeit der Osteoblasten und Osteoklasten vor. Die Ratten, die Dosen von 2,000 r bzw. 3,000 r

erhalten hatten, wurden moribund oder starben im Laufe von 8—10 Tagen, wobei sich Nekrose und Ablösung des oralen Epithels zeigte.

In der zweiten Gruppe entstanden zweierlei Läsionen. Bei der einen war eine ausgesprochene Zerstörung des Parodontiums des ersten oder dritten Molars kennzeichnend, während das Parodontium der übrigen Molaren relativ unbeschädigt geblieben war. Diese Verletzungen hatten in Ulzerationen der umgebenden Schleimhaut ihren Ausgangspunkt. Die anderen Verletzungen wiesen weniger ernsthafte Veränderungen auf und entstammten dem eigentlichen parodontalen Gewebe, sie gaben sich durch fehlende Proliferation des interdentalpapillären Epithels, durch eine gehemmte Entzündungsreaktion, durch Zusammenballen kollagener Substanz und schliesslich durch herabgesetzte Osteoblast- und Osteoklastfunktion zu erkennen.

Es wurden in den Rattenkiefern Fälle von Röntgenosteomyelitis gefunden, doch konnte diese Erkrankung nicht als eine direkte Folge derjenigen des parodontalen Gewebes angesehen werden.

REFERENCES

Aub, J. C., R. D. Evans, L. H. Hempelmann, & H. S. Martland, 1952: The late effects of internally-deposited radioactive materials in man. Medicine (Baltimore) *31:* 221—329.

Burstone, M. S., 1950 a: The effect of radioactive phosphorus upon the development of the teeth and mandibular joint of the mouse. J. Amer. dent. Ass. *41:* 1—18.

—»— 1950 b: The effect of X-ray irradiation on the teeth and supporting structures of the mouse. J. dent. Res. *29:* 220—231.

—»— 1950 c: Studies on the effect of radioactive colloidal gold on the development of the oral structures of the mouse. Arch. Path. *50:* 419—426.

—»— 1951: Studies on the alterations of development of the teeth and adjacent structures following local administration of chromic phosphate containing P^{32}. J. Amer. dent. Ass. *42:* 418—423.

Chambers, F., E. Ng, H. Ogden, G. Coggs, & J. Crane, 1958: Mandibular osteomyelitis in dogs following irradiation. Oral Surg. *11:* 843—859.

Dale, P. P., 1953: The effect of X-ray irradiation on the rat incisor. J. dent. Res. *32:* 117—125.

Dale, P., 1957: Radiological effects in the rat dentition. Proc. 25th Year Celebr. Univ. Rochester Dental Branch Fellowship Program 1955.

English, J. A., M. G. Wheatcroft, H. W. Lyon, & C. Miller, 1955: Long term observations of radiation changes in salivary glands and the general effects of 1,000 r to 1,750 r of X-ray radiation locally administered to the heads of dogs. Oral Surg. *8:* 87—99.

Ellinger, F., 1957: Effects of ionizing radiation on the oral cavity. Chapter 18 in: *F. Ellinger* (Ed): *Medical Radiation Biology*. C. C. Thomas, Springfield, U. S. A.

Fedorov, N. A. & A. A. Prokhonchukov, 1959: Experiments in obtaining periodontal lesions in rats by the effect of ionizing radiation (in Russian). Stomatologiya (Mosc.) *2:* 3—7.

Frandsen, A. M, 1962: Effects of roentgen irradiation of the jaws on socket healing in young rats. Acta odont. scand. *20:* 307—333.

Gotthard, P. P., 1923: Über Zahnschädigungen nach Röntgenbestrahlungen. Fortschr. Röntgenstr. *30:* 139—142.

Gowgiel, J. M., 1960: Experimental radio-osteonecrosis of the jaws. J. dent. Res. *39:* 176—197.

Greulich, R. C. & B. H. Ershoff, 1961: Delayed effects of multiple sublethal doses of total body X-irradiation on the periodontium and teeth of mice. J. dent. Res. *40:* 1211—1224.

Leist, M, 1926: Experimentelle Untersuchungen über die Einwirkung der Röntgenstrahlen und des Radiums auf die zweite Dentition. Z. Stomat. *24:* 452—460.

—»— 1927: Über die Einwirkung der Röntgenstrahlen und des Radiums auf Zähne und Kiefer. Strahlentherapie *24:* 268—281.

Medak, H. & G. W. Burnett, 1954: The effect of X-ray irradiation on the oral tissues of the Macacus Rhesus monkey. Oral Surg. *7:* 778—786.

Ng, E., F. W. Chambers, H. S. Ogden, G. C. Coggs, & J. T. Crane, 1959: Osteomyelitis of the mandible following irradiation. Radiology *72:* 68—74.

Quastler, H., M. H. Austin, & M. Miller, 1956: Oral radiation death. Radiat. Res. *5:* 338—353.

Regaud, C., 1922: Sur la Sensibilité du Tissue osseux normal vis-a-vis des Radiations X et γ et sur le Méchanisme de l'Ostéoradionécrose. C. R. Soc. Biol. (Paris) *87:* 629—632.

Rosenthal, M., 1937: Experimental radium poisoning. II. Changes in teeth of rabbits produced by oral administration of radium sulphate. Amer. J. med. Sci. *193:* 495—501.

Sicher, H. & J. P. Weinmann, 1944: Bone growth and physiologic tooth movement. Amer. J. Orthodont. *30:* 109—132.

Stafne, E. C. & H. H. Bowing, 1947: The teeth and their supporting structures in patients treated by irradiation. Amer. J. Orthodont. *33:* 567—581.

Zerosi, C., 1938: Experimentelle Untersuchungen über Reaktionen und histopathologische Veränderungen, welche durch Röntgen- und Radiumbestrahlungen in dentalen und periodontalen Gewebe verursacht werden. Zahnärztl. Rdsch. *47:* 265—272.

—»— 1940: Experimentelle Forschungen über die histologischen Reaktionen und Veränderungen der dentalen und peridentalen Gewebe infolge von Röntgen- und Radiumbestrahlung. Z. Stomat. *38:* 278—304, 322—339.

PLATES

Plate 1.

Interdental tissues in control rats, 65 to 95 days old. Hematoxylin-eosin stain

A. Interdental papilla displaying a minimum of epithelial proliferation and round cell infiltration. Original magnification X 64.

B. Interdental papilla with proliferating epithelial cells interspersed with edema and inflammatory cells. Original magnification X 64.

C. Interdental papilla exhibiting epithelial proliferation, moderate round cell infiltration, and lysis of the subepithelial collagen fibres. Original magnification X 64.

D. Interdental papilla with epithelial proliferation and round cell infiltration as a reaction to foreign body impaction. Original magnification X 64.

E. Proliferating gingival epithelium seen as "islands" in the periodontal membrane. Original magnification X 64.

F. A periodontal abscess situated between the second and third molars. Original magnification X 26.

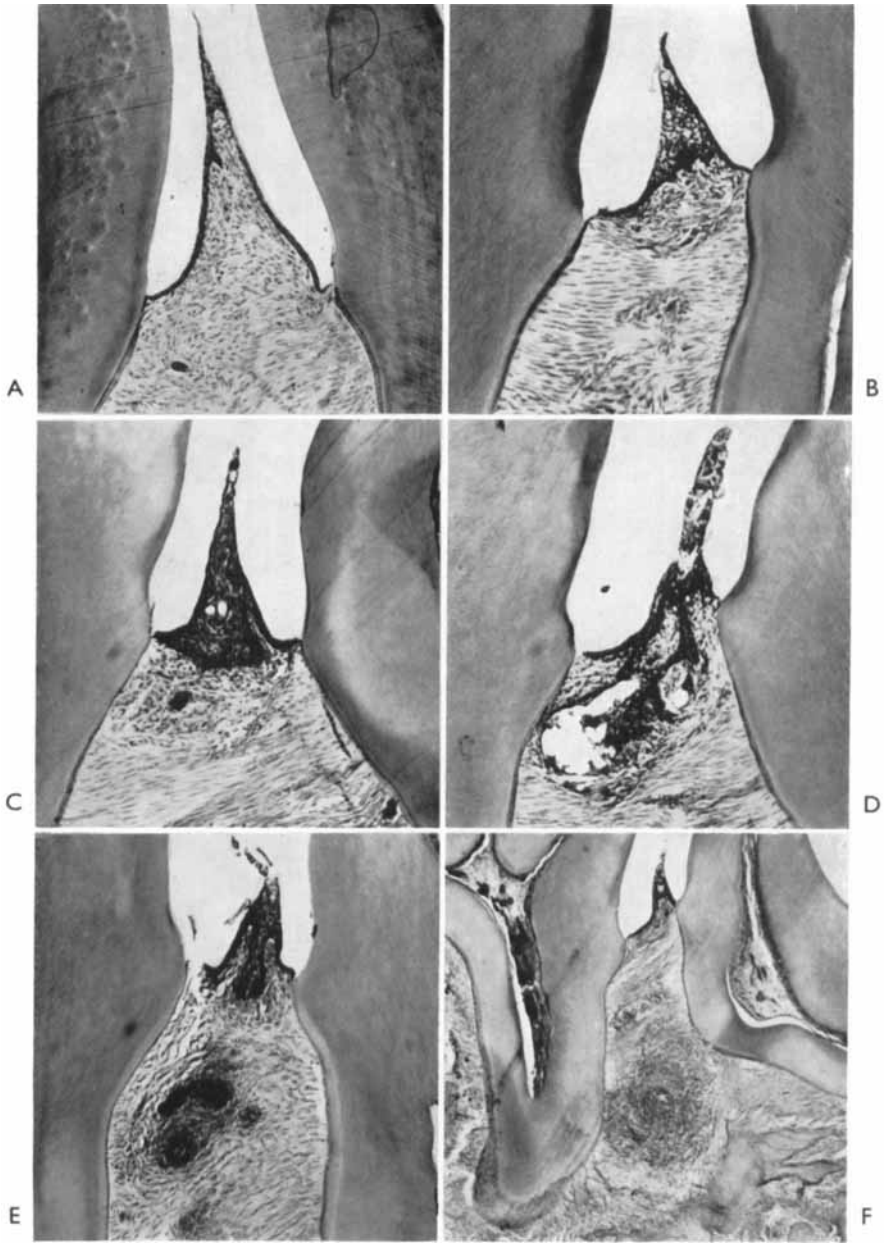

A
B
C
D
E
F

Plate 2.

Alveolar bone and periodontal membrane in 65 day old control rats. Hematoxylin-eosin stain.

A. Central section through a lower first molar. A large marrow cavity is noted. Original magnification X 26.

B. The same tooth as in Fig. A sectioned further buccally. Little marrow is seen. Original magnification X 26.

C. Distal root surface and adjacent alveolar bone. Resorption of tooth and bone, and lack of orientation of cells and fibres in the periodontal membrane. Original magnification X 260.

D. Mesial root surface and adjacent alveolar bone. Apposition of bone and cementum, and definite orientation of cells and fibres in the periodontal membrane. Original magnification X 260.

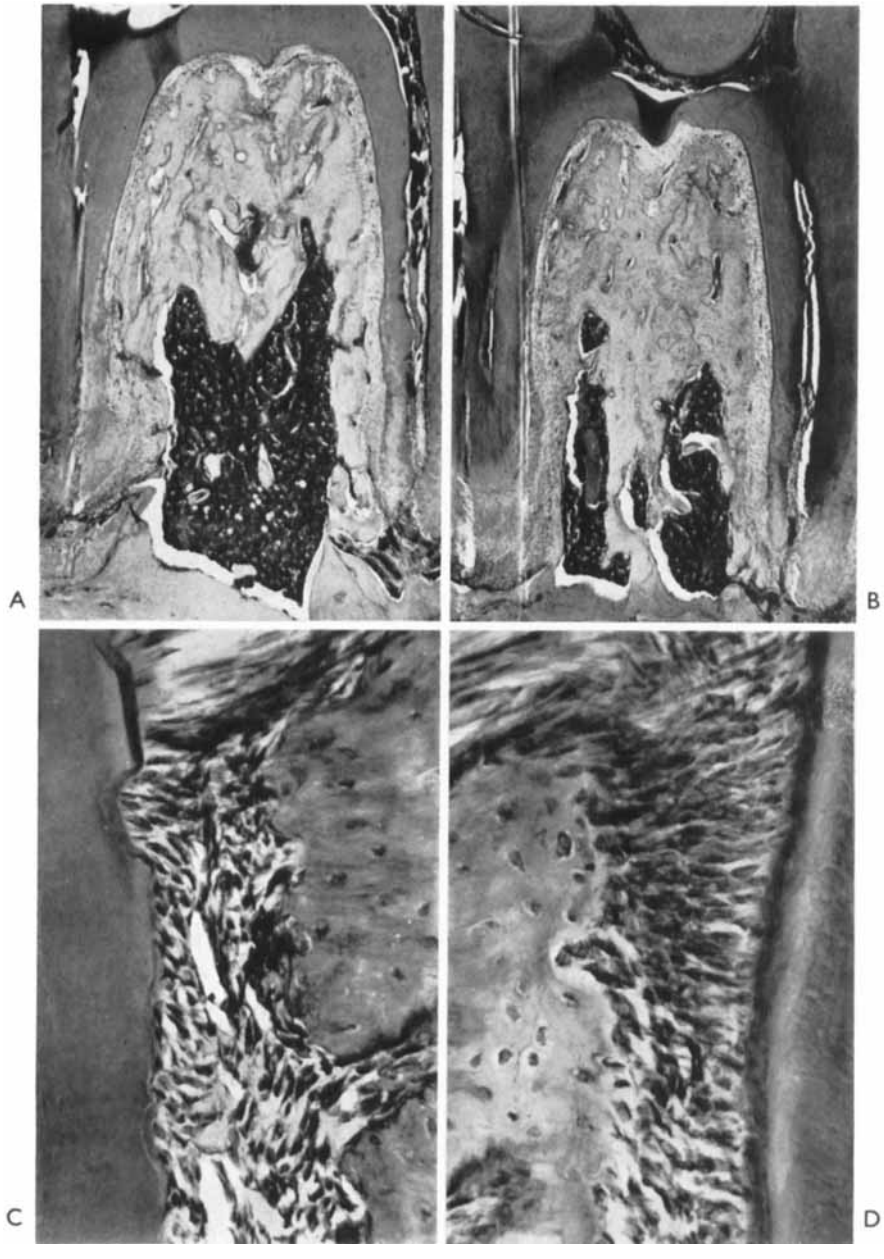

A
B
C
D

Plate 3.

Periodontal tissues in rats irradiated on the molar regions. Hematoxylin-eosin stain. Original magnification X 15.

A. Ulcerations of tongue and mucous membrane anterior to a lower first molar 12 days after the irradiation. Exudation at the gingival margin and fibrous transformation of the marrow.

B. Ulceration and necrosis of the entire area anterior to a lower first molar 48 days after the irradiation. Extension of the process to the interradicular tissues associated with pronounced bone resorption.

C. Ulceration and necrosis of the periodontium of a lower third molar and adjacent soft and hard tissues 47 days after the irradiation.

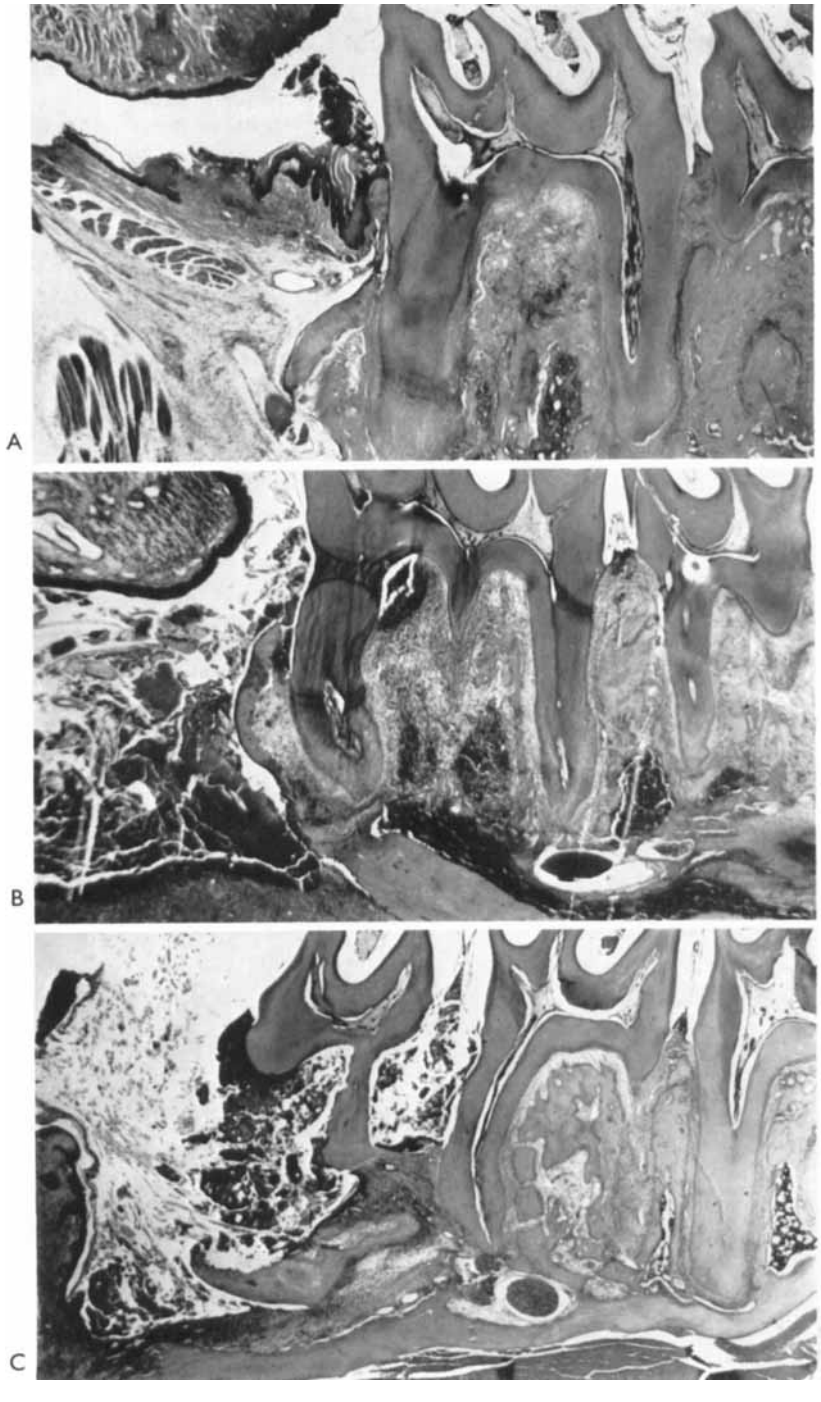

A
B
C

Plate 4.

Periodontal tissues in rats irradiated on the molar regions.

A. Interdental papilla 48 days after the irradiation. Atrophy of the epithelium and diminished round cell infiltration of the subepithelial tissue. Hematoxylin-eosin stain. Original magnification X 64.

B. Interdental alveolar septum 13 days after the irradiation. Absence of the normal apposition-resorption pattern. Hematoxylin-eosin stain. Original magnification X 64.

C. The gingiva mesial to a lower first molar 12 days after the irradiation. Plaque is present on the surface, and there is pronounced edema of the subepithelial tissue. Hematoxylin-eosin stain. Original magnification X 64.

D. The gingival margin mesial to a lower first molar 12 days after the irradiation. Clumping of the collagen. Van Gieson's stain. Original magnification X 260.

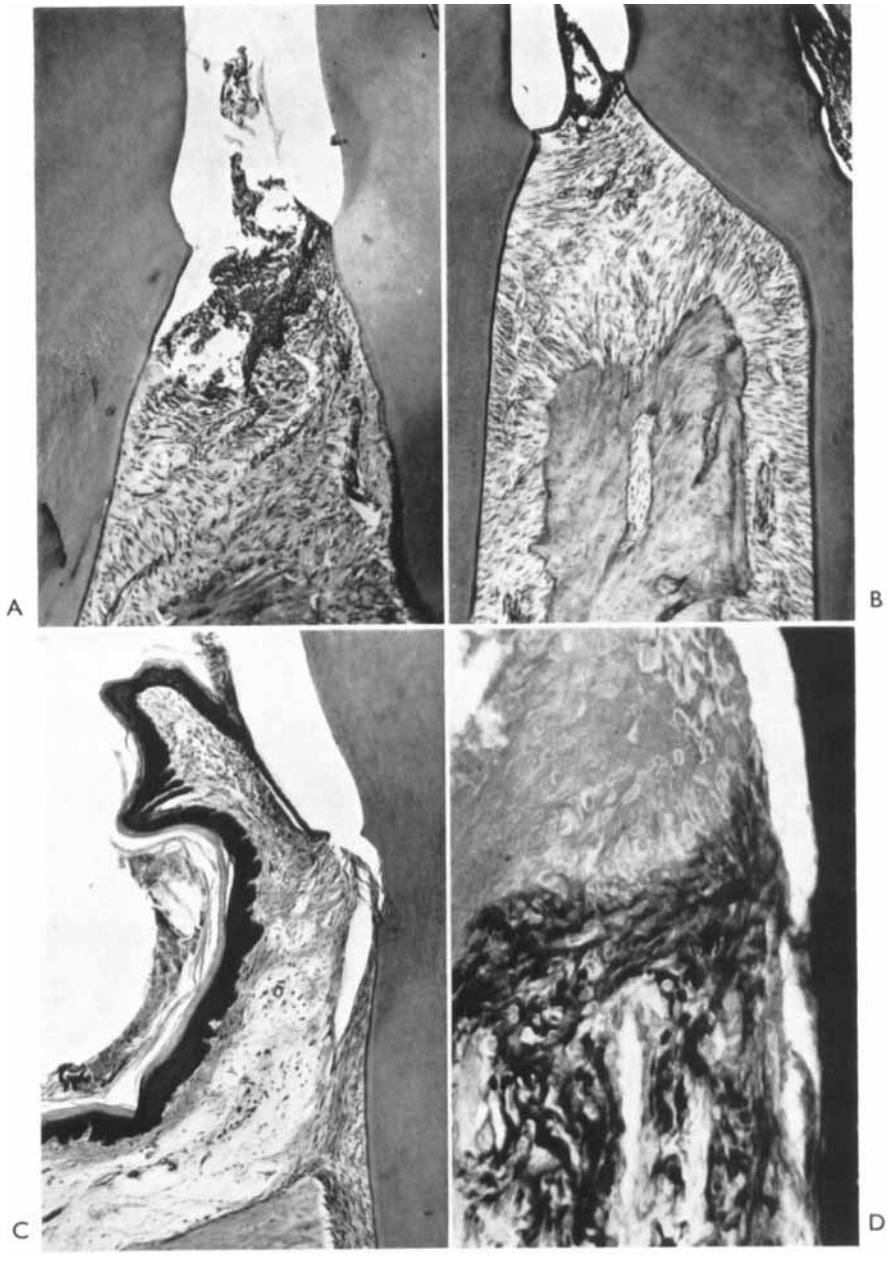

A
B
C
D

Plate 5.

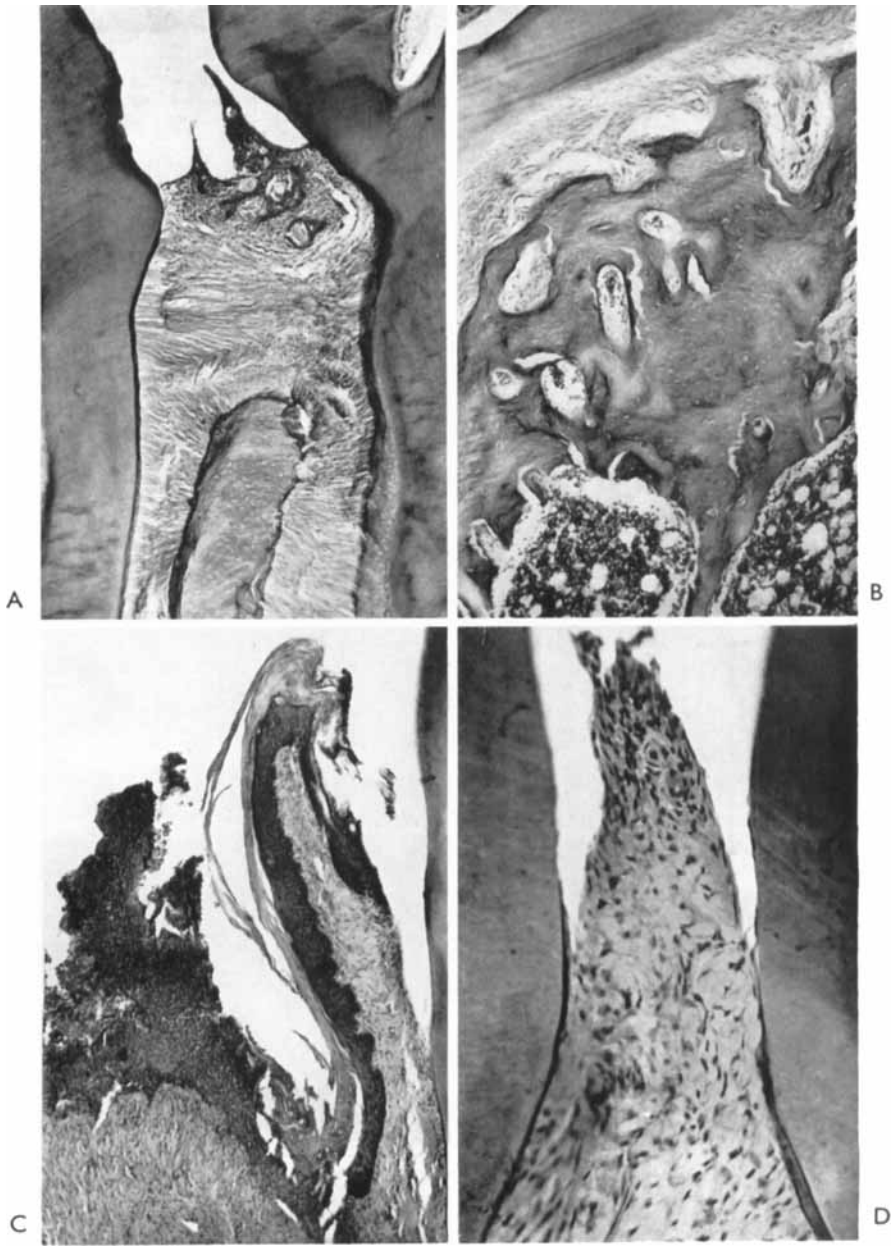
Periodontal tissues in rats irradiated on the head. Hematoxylin-eosin stain.

A. Interdental papilla and alveolar septum 93 days after irradiation with 1,000 r. Epithelial proliferation and subepithelial round cell infiltration. Reduced cellularity of the periodontal membrane. Osteocytes with pyknotic nuclei. Original magnification X 64.

B. Interradicular alveolar bone 38 days after irradiation with 1,000 r. The osteocytes display hyperchromatic and pyknotic nuclei. Original magnification X 64.

C. The gingival margin mesial to a lower first molar nine days after irradiation with 2,000 r. The connective tissue of the adjacent mucous membrane deprived of epithelium and covered by a purulent exudate. Original magnification X 64.

D. Interdental papilla eight days after irradiation with 3,000 r. Loss of epithelium and lack of inflammatory reaction. Original magnification X 260.


A
B
C
D