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RADIOTHERAPY AND CHEMOTHERAPY FOR DOMESTIC ANIMALS

III. The treatment of non-malignant conditions in dogs and cats

by

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Chronic inflammatory lesions are common in animals, and are often ver. resistant to medical and surgical treatment. The resolution of indolent ulcers in man is sometimes hastened by small doses of roentgen rays and it seemed reasonable to explore their effects on similar lesions in domestic animalsy An account of the response to γ rays of such lesions, in bone and soft tissues of the horse, has already been published (SILVER & CATER 1964 a); in the present paper, the results of the irradiation of various chronic inflammatory lesions in dogs and cats, with roentgen and β rays, are reported. These lesions are especially common around the mouth, where they are subjected to constant irritation and trauma from licking. They are also frequent in the ears of dogs, owing to the rubbing of corrugations of the external auditory meatus against each other. Exostoses are usually found as a result of trauma, but spinal arthritis with periarticular bony outgrowths often occur in long-backed dogs. Keratitis

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is a very common disease in dogs, as their eyes are generally more exposed to such irritants as dust and grit than are human eyes. The disease often becomes chronic and ulceration of the cornea is a frequent complication. In many cases, where extensive vascularisation of the cornea has developed, the lesions show considerable resistance to orthodox medical treatment.

Technique. The problems involved in the application of roentgen therapy to animals have been discussed by SILVER & CATER (1964 b). Filtration was arranged to give maximum irradiation to the lesion.

Beta ray therapy was carried out by using a flat 1.5 cm disc, ^{90}Sr applicator, on the end of an aluminium handle, delivering 112 rad/sec. The animals were anaesthetised, the eyelids held open with an eye speculum and the eye held in the desired position by tension sutures through the scleral conjunctiva. During anaesthesia there was invariably a powerful ventromedial rotation of the eyeball which almost completely hid the cornea. The third eyelid was retracted with forceps. The surface of the cornea was lubricated with an aqueous local anaesthetic solution before the ^{90}Sr was applied to the eye. It was found convenient to insert the applicator under the eyelids but in some dogs the palpebral aperture was too small for this manoeuvre, and then some skin reaction and epilation of the edges of the eyelids was seen; it was never permanent, however.

Where the lesion was more than 2 mm thick, it was removed completely, or shaved down to a thin layer, before the application of the β rays. This was particularly necessary in the case of some dermoids.

The curvature of the eye, even in a large dog, is such that a flat applicator will only contact the cornea over a very short distance. To obviate the danger of high dosage at one point and an inadequate dose on the periphery of the lesion, the applicator was rocked with a circulator motion to ensure that it contacted the eye over its whole area. Care was taken not to cause mechanical damage to the corneal epithelium by such movements.

Results

Roentgen therapy. Typical responses of chronic inflammatory tissues in dogs and cats to treatment with roentgen rays are illustrated by the following case histories.

Case 1. Alsatian dog, M. 5 years, had a chronic granulating fibrotic ulcer (7 × 5 cm) on the side of nose and face, with a 3-year-history of slow spread. Treatment: 220 kV roentgen rays, 7 × 7 single field, 0 Cu/1 Al, MTD 250 r followed by nobecutane spray to minimise trauma from licking. The ulcer shrank to one third of its original size in 6 to 8 weeks. Further treatment was refused and some ulceration persisted for 6 months.

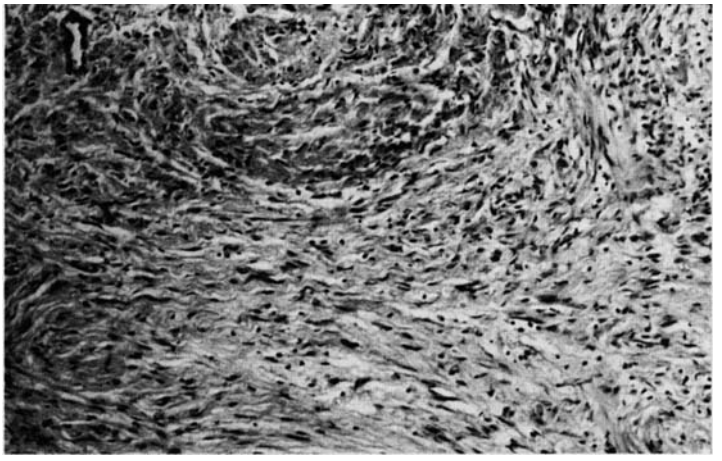


Fig. 1. Photomicrograph of chronic granulating ulcer of the nose of a dog (Alsatian, Case 1). H & E. × 170.

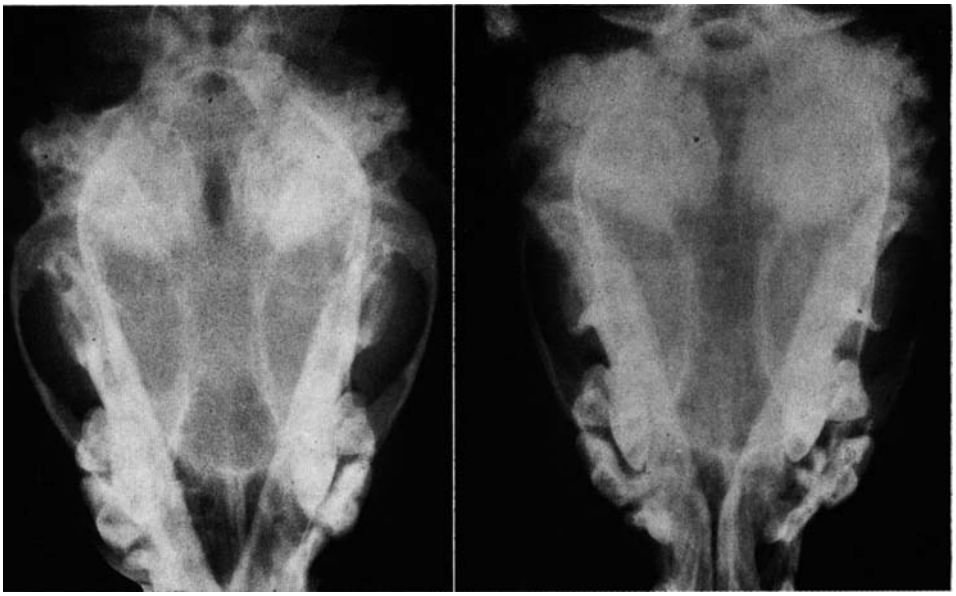
Case 2. Cat, M. 5 years, had a persistent ulcer (3 × 2 cm) on the upper lip and the nose, with 1 × 1 cm extension to the lower lip; it had failed to respond to repeated surgical and medical treatment over 2 years. Radiotherapy with 220 kV roentgen rays, 3.5 cm frontal field, 0 Cu/1 Al, MTD 250 r, and 2.5 cm right lateral field, 1 Cu/1 Al, MTD 250 r, resulted in slow healing of the ulcer which was complete in 334 days.

Case 3. Cat, F. 7 years, with a persistent ulcer 1 × 2.5 cm on the upper lip treated with 220 kV roentgen rays, 3.5 cm ⊙ frontal field, 1 Cu/1 Al, MTD 250 r. The ulcer healed in 60 days. Previous medical and surgical treatment over a year had been unsuccessful.

Case 4. Labrador dog, M. 7 years, with an ulcer (3 × 2 cm) of the nose and nasal septum, persisting for more than a year. Radiotherapy with 220 kV roentgen rays, 5 cm ⊙ 2 opposing fields, 1 Cu/1 Al, CTD 250 r, was followed by slow healing. A two thirds reduction of the area occurred in 52 days. Healing was complete in 78 days.

Case 5. Alsatian, M. 3 years, with chronic sinus discharge (3 × 4 cm) developed after removal of impacted left para-anal sacs. After failure of medical and surgical treatment, radiotherapy with 220 kV roentgen rays, 5 cm ⊙ frontal field, 0 Cu/1 Al, MTD 390 r, on day 0 and 910 r on day 119, was followed by some improvement. The animal developed a second sinus on the right side and was subsequently destroyed as it became savage. The treated sinus never healed completely.

Case 6. Alsatian, M. 7 years, with a similar lesion (4 × 4 cm) and history as in Case 5. It was treated with 220 kV roentgen rays, 5 cm ⊙, 0 Cu/1 Al, MTD 320 r on day 0 and 800 r on day 150, which resulted in a very slow filling of the cavity with healthy granulation tissue. Healing was obvious after each treatment but complete resolution did not occur till day 317.



a b

Fig. 2. Roentgenograms of skull of dog (Case 9). a) At the age of 9 months, and b) at the age of 2 years (15 months after treatment with 755 r of 220 kV roentgen rays).

Case 7. Spaniel dog, M. 11 years, with a chronic fibrotic granuloma (6 × 6 × 2 cm) of hard palate with extensions to upper lip and nose. It had recurred twice after surgery, bled constantly and interfered with respiration. Treatment was given with 220 kV roentgen rays, 15 × 10 cm, 1 Cu/1 Al, in 3 fields: frontal 990 r, right, lateral 335 r and left lateral 335 r giving CTD 1 660 r. The mass shrank slowly and the general condition of the dog improved. At day 250 the animal was destroyed because of age and general infirmity. The lesion was still present but inactive and heavily fibrosed.

Case 8. Alsatian, M. 2 years: post-traumatic exostoses of radiocarpal, intercarpal and carpometacarpal joints, over 5 × 5 cm, with some limitation of carpal flexion to half of normal movement, 16 months after a road accident. Treatment with 220 kV roentgen rays to a 7 × 7 cm frontal field, 0 Cu/1 Al, MTD 240 r resulted in improved carpal flexion after 170 days and full movement after 330 days.

Case 9. West Highland dog, F. 9 months with bilateral exostoses of the petrous temporal bones and posterior borders of mandible, associated with excessive salivation and difficulty in swallowing. Radiotherapy with 220 kV roentgen rays, 5 cm ⊙, 0 Cu/1 Al, two lateral fields giving MTD 755 r to each petrous bone, was followed by no further extension of bony outgrowths and improved jaw movement. Excess salivation persisted.

The commonest lesions treated were ulcers around the mouth. In 4 of 5 cases there was a diminution in size of the ulcer following radiotherapy with doses of 250 r, and in 3 of these 4 there was complete resolution. The fifth case (Case 7) was a chronic granuloma with extensive fibrosis. This was treated with a much larger dose (CTD 1 660 r), which had a beneficial effect. The lesion became smaller and inactive but never healed.

Cases 5 and 6, with ulceration of the anal sacs, represent a common condition in dogs. These ulcers are constantly contaminated by faeces and are irritated by rubbing from the tail. They are often very resistent to orthodox treatment. Radiotherapy appeared to accelerate healing of these ulcers but the response was not very spectacular.

The effect of roentgen rays on two non-malignant bony conditions in dogs is illustrated by Cases 8 and 9. The former showed a periosteal reaction after trauma which limited carpal movement. A small dose of 220 kV roentgen rays (320 r) with 1 mm Al filtration was followed by cessation of further growth of exostoses, remodelling of the new bone already present, and restoration of carpal movements. Case 9 is of a completely different kind. The bilateral outgrowths of the petrous part of the temporal bone appear to have some genetic basis. The condition was known to have occurred previously in the family of this particular dog — it had been lethal because movement of the lower jaw eventually became impossible. The small dose of radiation (755 r with 1 mm Al filtration) was tried as an experiment and was followed by cessation of the growth of the bone. However, the animal was near the age when natural growth of the skull would be expected to cease anyway.

Beta ray therapy. This has been applied to a variety of eye conditions in dogs, especially those involving extensive vascularisation of the cornea and dermoid cysts. The number of cases treated, the doses given and the results obtained with the various lesions, are given in a Table.

Superficial vascularisation (pannus) was often so extensive as to render an animal completely blind and in the majority of cases was present in both eyes. These cases usually responded well to treatment, which was carried out in 3 or 4 fractions at intervals of 2 to 3 weeks. It was noted that if longer intervals were used, the response was less satisfactory — but it was not possible to use shorter intervals on more than a few (5 cases) as most of the animals came from considerable distances. In the few cases treated with 3 fractions at 4-day intervals the response was not obviously better. The first signs of regression of blood vessels was seen 2 to 4 weeks after the initial treatment and complete clearing of the cornea usually took from 6 to 8 weeks. It was noticed in several cases (9 out of 24) that although the keratitis resolved, the accompanying con-

Table

Response of eye lesions to radiotherapy

Lesion	Number of cases	Dosage in rad	Response to treatment			Recurrence within a year
			Complete remission	Some improvement	Nil	
Pannus	27	9 000—12 000	23	1	3	8
Interstitial keratitis	19	4 × 3 000	8	4	7	3
Dermoid cysts	6	2 × 3 000	5	—	1	—
Keratitis pigmentosa	6	3 × 3 000	0	4	2	3

junctivitis did not. In 8 of these 9 cases there was a recurrence of the keratitis at intervals ranging from 4 to 18 months after the first treatment. Four cases out of these 8 have shown repeated recurrence of superficial vascularisation, which regressed after each treatment but reappeared again in 8 to 12 months. Pigmentation in the areas previously covered by pannus has been seen in 12 out of 24 cases which responded to treatment. These 12 include all 8 of those in which there were recurrences. It is not clear if this pigmentation is deposited merely in the course of the resolution of chronic inflammation, or if it is accentuated by the radiation.

The response of interstitial keratitis is not so satisfactory, and deep blood vessels do not appear to be so affected by beta rays as blood vessels in the corneal conjunctiva. Very frequently, the smaller vessels regress but the larger ones do not. However, as there is some improvement in more than 50 % of cases, it seems reasonable to try β-ray therapy on this condition.

Dermoid cysts. The animals in which these occurred were all young. Direct irradiation of the cysts was followed by cessation of growth but there was little or no regression except in one case. The best results were obtained by irradiation of the tumour site following surgical removal of the majority of the growth. The dermoids which are listed in the table had all recurred after surgery.

Keratitis pigmentosa. This condition gave a poor response to beta ray therapy. It had been present for 1 to 2 years in all cases treated and in no case was there complete remission. Four of six cases showed some response but this was confined to a reduction of the vascularity, and there was no indication of removal

of pigment. Conversely, there was no obvious increase in pigment. Most of the cases which showed improvement relapsed within one year of the first treatment with β-rays.

Discussion

Radiation therapy for non-malignant conditions in animals seems justified when orthodox medical and surgical treatment has failed. The risk of inducing leukaemia by radiation therapy can be taken with greater equanimity in the case of an animal as opposed to human subjects.

The useful clinical effects of small doses of roentgen rays, such as are reported here, are difficult to explain. In the case of indolent ulcers the radiation seems positively to stimulate epithelialisation, and it presumably slightly alters the delicate balance between granulation tissue and skin, in favour of the latter. In horses, where exuberant granulation is a much greater problem than in the dog, much larger doses of radium γ-rays have had to be used to discourage connective tissue proliferation in chronic wounds.

The case of the puppy with exostoses of the petrous bones is interesting because of the familial history of the condition. It is open to question whether the radiation was responsible for arresting the growth of the bone or whether the exostoses stopped growing naturally at the same time as skull growth was completed. It is hoped to be able to repeat the treatment on a younger animal from this family to see if a low dose of radiation during the period of active skull growth will arrest the development of the exostoses. The case of post-traumatic exostosis (Case 8) responded in much the same way as similar lesions which we have treated in horses.

Another common condition of dogs, chronic otitis externa with ulceration and proliferation, is also alleviated by radiotherapy but as it is easily treated by surgery, which usually results in a permanent cure, it is hardly justifiable to use roentgen rays unless surgery is definitely contra-indicated.

The application of β-ray therapy to lesions of the eye has been reported by FRIEDELL, THOMAS & KROHMER (1951), LEDERMAN (1952, 1956, 1957), SEALE (1953), MERRIAM (1956), TROTT & WHEATLEY (1956), and FRASER & NAUNTON (1961) in man, and by CANDLIN & LEVINE (1952), CATCOTT & GREISNER (1954) and DALTON (1958) in the dog; and by CATCOTT, THARP & JOHNSON (1953) and WHEAT, BLACK, HAGE & RHODE (1954) in cattle and horses. Our results are broadly similar to those already reported but we found that at least 3 weeks elapsed before any response was discernible in cases of keratitis, which is in contrast to the 3 to 7 days mentioned by DALTON (1958) for the same conditions. CANDLIN & LEVINE (1952) used very large doses (20 000 rad) in

a single application, but in the few cases in which we gave 10 000 rad at once there was considerable radiation reaction 10 to 12 days later.

The danger of producing permanent damage to the eye by radiation largely concerns cataract formation. Cataract is common in old dogs and especially in those with diabetes. The range in tissue of β-radiation from ^{90}Sr is too short for more than a small percentage of the dose to reach the lens. With γ radiation or 220 kV roentgen rays the safe dose has yet to be determined. In man, CHARTERIS (1940) reports that damage to the lens is a rarity after a dose of 1 500 r and a certainty after 2 800 r. ALDEN, JONES & RANKIN (1949) used doses of up to 1 000 r for corneal ulcers without trouble, and SEALE (1953) treated 16 cases of carcinoma of the corneal limbus in man with 2 500 to 3 525 r radium γ rays and calculated the dose to the lens which varied between 800 and 1 380 r in the different cases. They state that no damage occurred to the normal adult lens. However, COGAN & DREISLER (1953) reported that one out of three patients given 600 r 200 kV roentgen rays will develop cataract, and MERRIAM & FOCHT (1957) found that the minimum cataractogenic dose was 200 r. SILVER & CATER (1964 b) irradiated both eyes of a dog with 940 r 220 kV roentgen rays and a year later repeated the treatment with 960 r. No cataract formation has been observed.

With regard to β-radiation of the eye, FRASER & NAUNTON (1961) report good results after 1 000 to 2 000 rep in human cases where the vascularisation of the cornea is superficial as in acne rosacae keratitis but much less effect when the vascularisation was of the deeper vessels, which is in agreement with our findings. With regard to the late effects of beta radiation on the eye, MERRIAM (1956) reported radiation cataract after 2 300 to 22 000 rep, telangiectasis after 3 000 to 5 000 rep, superficial keratinisation of the conjunctival epithelium (5 000 to 10 000 rep), superficial punctate keratitis (5 000 rep), iritis, iris atrophy, vascularisation and scarring of the cornea after much larger doses (20 000 to 30 000 rep).

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SUMMARY

Chronic non-malignant proliferative conditions in 7 dogs and 2 cats were treated with 220 kV roentgen rays. Beta radiation (6 000 or 12 000 rad) was used to treat eye conditions in 58 dogs (pannus 27 cases, interstitial keratitis 19, dermoid cysts 6, and keratitis pigmentosa 6).

ZUSAMMENFASSUNG

Chronische, nicht-maligne, proliferative Erkrankungen wurden an 7 Hunden und 2 Katzen mit 220 kV Röntgenstrahlen behandelt. Beta-Strahlen kamen zur Anwendung um bei 58 Hunden Augenerkrankungen zu behandeln (27 Fälle mit Pannus, 19 mit interstitielle Keratitis, 6 dermatoide zysten, 6 Fälle mit Keratitis pigmentosa).

RÉSUMÉ

Sept chiens et deux chats atteints d'affections chroniques proliférantes bénignes ont été traités par roentgenthérapie sous 220 kV. Des affections oculaires (pannus 27 cas, kératite interstitielle 19, kystes dermoïdes 6, et kératite pigmentaire 6) ont été traitées chez 58 chiens par les radiations bêta.

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