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INTRATRACHEAL INJECTION OF ANTIBIOTICS IN THE CALIFORNIA SEA LION, *Zalophus californianus*, AND BOTTLENOSED DOLPHIN, *Tursiops truncatus*

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Abstract: Gentamicin and cephaloridine were administered by intratracheal injection to the California sea lion, *Zalophus californianus*, and the bottlenosed dolphin, *Tursiops truncatus*. Uptake and clearance of these antibiotics in the blood were monitored. In all cases, absorption through the respiratory mucosa resulted in blood levels approaching therapeutic concentrations despite low dosages.

INTRODUCTION

For over a decade health management studies on captive marine mammals have been directed toward specific diseases, but few dealing with therapy.[2,3,7,9] Because these mammals live in water, the clinician must deal with some peculiar challenges: the animal's limited availability, thick fatty covering, and unique adaptations for deep diving.[7] In captivity, marine mammals are predisposed to acute and chronic respiratory infections,[5,9] requiring prompt and aggressive therapy. The standard methods of antibiotic administration, oral or intramuscular, commonly are insufficient in preventing mortalities.

Previous to this experiment, antibiotics had been delivered to the respiratory tract as aerosols using an ultrasonic nebulizer.[9] No measurable blood concentrations of gentamicin or chloramphenicol were found following such therapy. After determining aerosol droplet size, it was concluded that these antibiotics do not aerosolize sufficiently to afford clinical usage. Work with humans substantiates these findings.[12]

This paper deals with an administration method exposing antibiotics directly to the respiratory tract of dolphins and sea lions by intratracheal administration. Several recent studies in humans showed that high concentrations of polymyxin B[8] and gentamicin[4] could be attained in the sputum of humans following endobronchial and intratracheal administration. In one study, patients with bronchial infections responded more favorably to therapy administered intratracheally compared to the intramuscular route.[4]

MATERIALS AND METHODS

Gentamicin[1] and, in a separate experiment, cephaloridine,[2] were administered to California sea lions (*Z. californianus*) and Atlantic bottlenosed dolphins (*T. truncatus*) by direct injection into the trachea using a midline cutaneous approach over the trachea. For sea lions, a 2.5 cm 20 gauge needle was used and for dolphins a 7.5 cm 18 gauge needle was suitable. Antibiotics were diluted in sterile water to a volume of 6 ml in the sea lions and 8 ml in the dolphins. The dosages utilized were:

[1] Gentocin®, Schering Corporation, Kenilworth, New Jersey 07033, USA.

[2] Lordine®, Eli Lilly and Company, Indianapolis, Indiana 46206, USA.

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Antibiotic	Animal	No. of Animals	Dosages
Gentamicin	Sea lion	1	0.42 mg/kg
Gentamicin	Sea lion	1	0.75 mg/kg
Gentamicin	Dolphin	2	1.10 mg/kg
Cephaloridine	Sea lion	2	8.80 mg/kg
Cephaloridine	Dolphin	1	6.60 mg/kg

When the needle is properly placed in the trachea, air is aspirated and upon injection a slight cough is induced.

Serum was collected for antibiotic assay in sterile containers at 0, 1, 6, 12 and 24 hrs in the gentamicin experiments and 0, 1, 3, 6, 12 and 24 hrs in the cephaloridine studies. Within one hour of collection, the serum was frozen until analysis was initiated. A reference laboratory[3] performed the analyses using the spore plate agar diffusion method for gentamicin and cephaloridine.[9]

The distribution of injected fluid within the lung was tested using a fresh cavader *Z. californianus* lung which was maintained at a 45° angle to a horizontal surface in normal respiratory movements with a Bird Mark IX respirator.[4] Ten ml of aqueous barium sulfate[5] was injected into the trachea. After two minutes, radiographs of the lungs were taken to illustrate dispersion of the injectate.

RESULTS

The uptake and disappearance of gentamicin and cephaloridine in serum is presented for California sea lions in Figures 1 and 2, and for bottlenosed dolphins in Figures 3 and 4. In all experiments, sera contained measurable antibiotic levels at one hr after injection. In dolphins, at the manufacturers recommended dosage for humans, serum concentrations of gentamicin at one hr were above 2 μg/ml which is equivalent to to therapeutic levels for many susceptible bacteria.[11] A lower dosage was administered to sea lions with considerable lower serum levels resulting. With cephaloridine at a dosage between one-half and three-quarters the manufacturer's recommended intramuscularly administered dosage in humans, serum levels attained at one hr in both species were approximately one-third the systemic therapeutic level of 1-6 μg/ml.[11]

The distribution of the injectate following intratracheal injection is shown in Figure 5. Note that there was relatively equal diffusion throughout the lung. One might presume that, with the airway held at a more horizontal plane, the fluid might distribute at a higher concentration in to the anterior lung areas. It would appear, therefore, that infections throughout the lung may be effectively treated by this technique.

DISCUSSION

The data shows that both gentamicin and cephaloridine are absorbed through the respiratory mucosa with diffusion into the blood. Both of these antibiotics are effective against most gram negative and many gram positive bacteria found in respiratory infections of sea lions.[10] Since the injected antibiotic was here shown to rapidly descend into the distal lung airways, it may be assumed that prior to absorption into the blood, high local tissue concentrations of the drug occurs. These high antibiotic concentrations are desirable to treat otherwise unresponsive pulmonary infections. Drug excretion from the blood appears to be similar to that reported previously.[1] The trachea and peritracheal tissues have been examined at necropsy with no evidence of trauma to date. I have not had any animals expel more than one ml of the injected fluid.

[3] Bio-Science Laboratories, Van Nuys, California 91405, USA.
[4] Mark IX Respirator, Bird Corporation, Palm Springs, California 92262, USA.
[5] Oratrast®, Barnes-Hind Barium Products, Sunnyvale, California 94086, USA.

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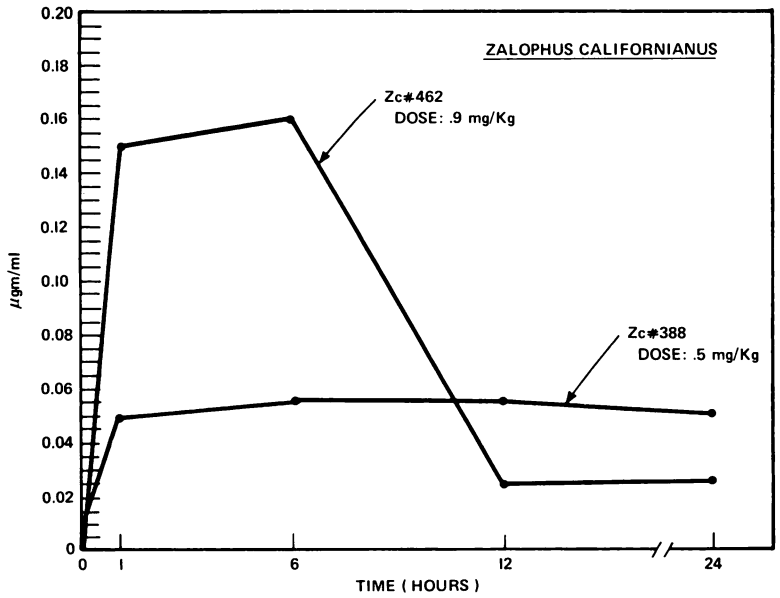


FIGURE 1. Serum levels of Gentamicin following intratracheal administration.

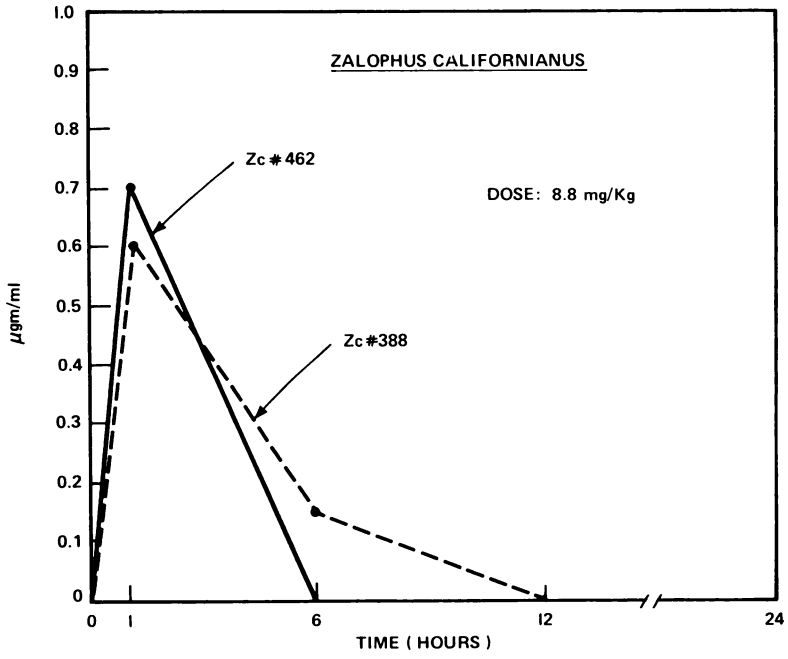


FIGURE 2. Serum levels of Cephaloridine folloiwng intratracheal administration.

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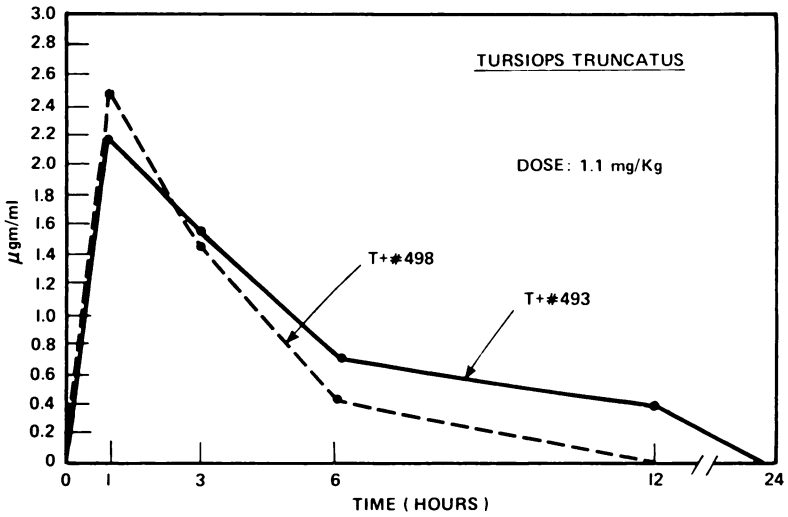


FIGURE 3. Serum levels of Gentamicin following intratracheal administration.

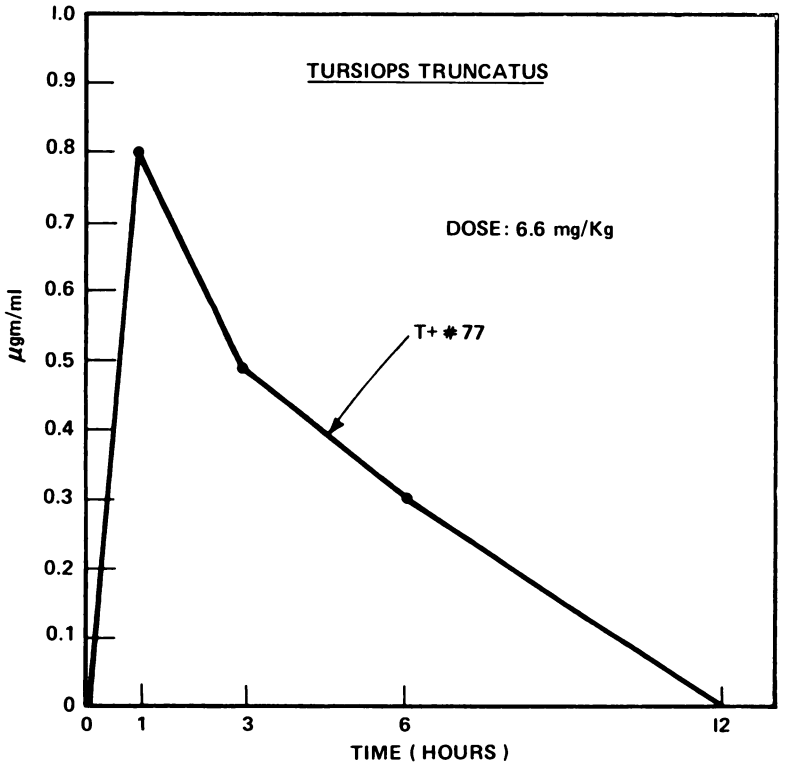
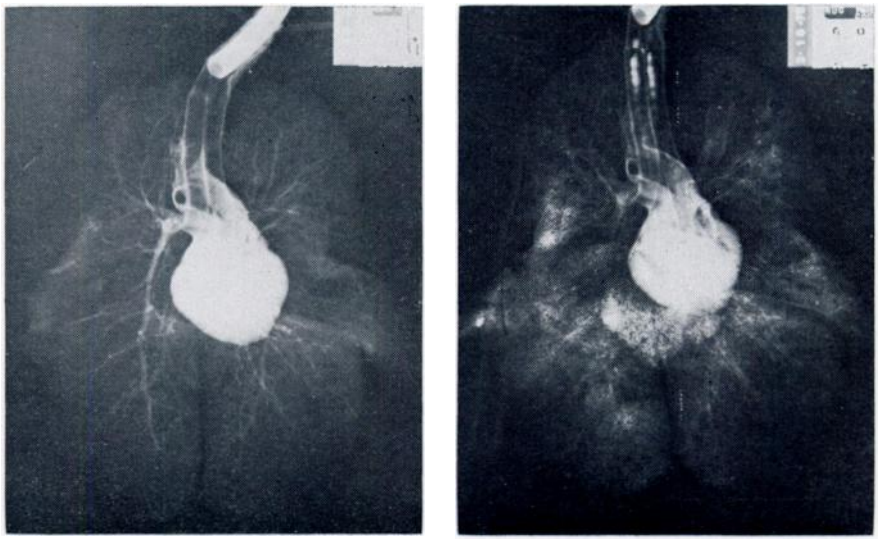


FIGURE 4. Serum levels of Cephaloridine following intratracheal administration.

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Normal Lung Post injection

FIGURE 5. Radiographs illustrating the distribution of barium sulfate within the cadaver sea lion lung following intratracheal administration.

The administration of either of the antibiotics reported here by the intratracheal routes in dolphins and sea lions suffering from compromising respiratory infections is considered routine by the author. In recent clinical applications, up to 20 ml of injectate has been administered intratracheally to sea lions averaging 50-75 kg without apparent stress. It is postulated that this larger volume of fluid results in greater dispersion of the antibiotic within the lungs. In at least 2 dolphins and 5 sea lions, this therapeutic technique was considered directly related to a successful clinical course.

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