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THERAPEUTIC TREATMENTS IN CANINE DISTEMPER WITH CHLOROMYCETIN AND AUREOMYCIN

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INTRODUCTION

It is already known that chloromycetin and aureomycin are not only extremely active against Gram-negative microorganisms, but also against certain Gram-positive microorganisms, rickettsiae, viruses and certain protozoa. So they possess a wide range of activity against the various pathogens. They are now well established as effective chemotherapeutic agents for many infectious diseases of animals.

Many authors[1,2,5,14,19,20] have found that, when these antibiotics were administered per orally, they were very effective against disturbances caused by the secondary infections in canine distemper, but were not beneficial in nervous type disturbances. There have been published only few reports in Japan of therapeutic experiments using chloromycetin[15,18] and aureomycin[9,16] in complicated canine distemper. The results of treatments were not found to be so effective in nervous type diseases as were reported in foreign papers. With the basic studies[1,6,7,12,13] on the therapeutic blood levels in chloromycetin and aureomycin treatments, it seems that they are to be used orally 15 to 50 mg/kg of body weight respectively divided to 3 or 4 times per day.

The present workers used these antibiotics for 35 dogs which showed clinically canine distemper with almost always what seemed to be complicated secondary infections. Workers attempted to investigate the clinical, hematological, bacteriological, parasitological and the pathological changes in the course of their study of these cases.

MATERIALS AND METHODS

For 15 cases chloromycetin therapy was carried out and for 20 cases aureomycin therapy. Ages were 1 to 12 months with a mean of 5.6 months. Body weights were 3 to 32 kg with a mean of 14.4 kg. Conditions of diseases were severe in almost all cases. In the first diagnosis, high temperature, poor or loss of appetite, depression, emaciation, anemia of mucous membranes, palpitation, cardiac

disturbance, nasal catarrh, pneumonia, gastroenteritis, conjunctivitis, pustular dermatitis and nervous disturbance were found respectively.

The dosage schedules of both antibiotics ranged from 20 to 50 mg/kg of body weight. They were administered orally in divided doses 4 times per day for 1 to 6 days and the aureomycin ointment was used topically. As additional treatments, glucose(5%)-ringer liquors and cardiotonicums were injected subcutaneously. Further, stomachia and digestiva were given orally in gastroenteritis and sinapism packing was applied to the case of pneumonia.

RESULTS OF EXPERIMENTS

From the clinical findings, patients were classified as suffering respiratory, digestive and the nervous type sicknesses.

1. Respiratory Type (Table 1)

Fifteen cases (43%) were found of the respiratory type; the characteristic symptoms were catarrhal pneumonia which was associated with high temperature, conjunctivitis, increase in breathing or dyspnea and catarrhal rhinitis.

TABLE 1. *Treatment of Respiratory Type in Canine Distemper*

GR.	DOG. NO.	SPEC.	AGE (Mon.)	BODY WEIGHT (kg)	SEVERITY OF DISEASE	REMARKABLE SYMPTOMS	DOSE PER DAY (mg/kg)	DAYS FOR ADMINIST.	TOTAL DOSES (g)	COURSE (days)
Chloromycetin	1	Sheph.	7	19	Slight	P. G. C.	20	3	1.14	6
	2	Setter	9	13	Severe	P. C. D.	20	5	1.56	7
	3	Ainu	8	21	"	P. C.	20	4	1.68	6
	4	Mongr.	7	13	"	P. C. D.	30	2	0.78	2
	5	Sheph.	12	32	"	P. G. C.	30	3	2.88	5
	6*	Setter	4	11	"	P. C. K.	30	3	0.99	15
	7	Sheph.	5	25	"	P. G. C.	30	5	6.25	8
Aureomycin	8	Mongr.	9	10	Severe	P. G. C.	20	4	0.80	6
	9	Sheph.	6	20	Slight	P. C. D.	25	2	1.00	3
	10	Mongr.	8	14	Severe	P. G. C.	25	3	1.05	5
	11	Sheph.	4	12	Slight	P. C. K.	25	2	0.60	5
	12	"	8	27	Severe	P. G.	25	2	1.35	5
	13	"	6	20	"	P.G.C.D.	50	2	2.00	5
	14	"	6	20	"	P. C.	50	2	2.00	6
	15	"	4	11	"	B. G. D.	50	2	1.10	3

Note: B (Bronchial catarrh), C (Conjunctivitis), D (Pustular dermatitis), G (Gastroenteritis), K (Keratitis), P (Catarrhal pneumonia).
No. 6 died but the other dogs recovered.

Seven dogs were subjected to chloromycetin therapy. When chloromycetin was administered with a mean of 28.6 mg/kg of body weight per day for 2 to 5 days, the suitable symptomatic treatments were conducted in accordance with the severity of the diseases. General conditions improved at 24 to 48 hours and 6 dogs recovered in 2 to 7 days, but 1 dog died in 15 days.

Aureomycin was used for the other 8 dogs; the conditions before treatments were almost identical with chloromycetin group. Aureomycin was administered with a mean of 33.7 mg/kg of body weight per day for 2 to 4 days and the symptomatic treatments were made as in the chloromycetin group. All recovered at 3 to 6 days after treatments.

2. Nervous Type (Table 2)

Fourteen cases (40%) were clinically recognized as nervous type sicknesses. The majority of patients in this type, symptomatic epilepsia, tic or signs of encephalitis were associated with catarrhal pneumonia or gastroenteritis. With the exception of antibiotic treatments symptomatic therapy was carried on.

Chloromycetin was used for 6 dogs with a mean of 37.5 mg/kg of body weight per day for 2 to 3 days. Three dogs died in 3 to 8 days, while in the other 3

TABLE 2. *Treatment of Nervous Type in Canine Distemper*

Gr.	Dog No.	Spec.	Age (mon.)	Body Weight (kg)	Remarkable Symptoms	Dose per Day (mg/kg)	Days for Administ.	Total Doses (g)	Course (days)
Chloromycetin	16	Mongr.	6	15	P. G. C.	25	3	1.125	9
	17	Ainu	4	8	P. G. C.	30	3	0.72	8
	18	Mongr.	6	8	P. G. C.	30	3	0.72	4
	19	Akita	3	9	G. C. E.	30	2	0.54	8
	20	Sheph.	4	8	G. E.	50	3	1.20	12
	21	Ainu	4	10	E.	50	3	1.50	3
Aureomycin	22	Mongr.	6	9	B. E.	20	1	0.18	2
	23	Sheph.	2	8.5	P.G.C.E.	20	4	0.68	5
	24	Spitts	1	3	E.	20	2	0.12	3
	25	Sheph.	7	26	G. C. E.	25	6	3.90	10
	26	"	4	12	P.G.C E.	25	4	1.20	5
	27	"	3	10	P.G.C E.	25	6	1.50	10
	28	Mongr.	4	12	G. E.	30	2	0.72	2
	29	Sheph.	3	10	P. C. E.	30	5	2.50	6

Note: B (Bronchial catarrh), C (Conjunctivitis), D (Pustular dermatitis), E (Symptomatic epilepsia), G (Gastroenteritis), P (Catarrhal pneumonia). The severity of disease of Nos. 16~29 was serious. Nos. 18, 19, 21~29 died and Nos. 16, 17 & 20 recovered but remained tic.

dogs, nervous symptoms excepting tic disappeared in 8 to 12 days and they recovered good health. Aureomycin was administered to 8 dogs with a mean of 26.8 mg/kg of body weight per day for 1 to 6 days. Beneficial results were not obtained and all died in 2 to 10 days.

3. Digestive Type (Table 3)

Digestive type sicknesses were found in 6 dogs (17%). They principally indicated gastroenteritis, but with associated pneumonia, conjunctivitis and pustular dermatitis.

Chloromycetin was administered for 2 dogs 30 mg/kg of body weight per day for 4 days and aureomycin was used for 4 dogs 20 to 30 mg/kg per day for 2 to 5 days. The symptomatic treatments were also given as was done in the other 2 groups. The diseases became slight after 1 to 2 days and all recovered in 3 to 6 days.

TABLE 3. *Treatment of Digestive Type in Canine Distemper*

Gr.	Dog No.	Species	Age (mon.)	Body Weight (kg)	Severity of Disease	Remarkable Symptoms	Dose per Day (mg/kg)	Days for Administ.	Total Doses (g)	Course (days)
Chloromycetin	30	Karahuto	3	15	Slight	G. C. D.	30	4	1.80	4
	31	Mongrel	4	5.5	Severe	G. P. C.	30	4	0.66	4
Aureomycin	32	Mongrel	8	12	Severe	G. C. K.	20	5	1.20	6
	33	Settre	8	15	Slight	G. R.	20	2	0.60	3
	34	Pointer	6	18	"	G.	25	2	0.90	4
	35	Shepherd	6	26	"	G. C.	30	2	1.56	5

Note: C (Conjunctivitis), D (Pustular dermatitis), G (Gastroenteritis), K (Keratitis), P (Catarrhal pneumonia), R (Catarrhal rhinitis).
* All the animals recovered.

4. Topical Use of Aureomycin Ointment

Twenty-five dogs having conjunctivitis, 6 dogs having pustular dermatitis and 8 dogs having keratitis were employed for treatment with aureomycin ointment. By the ophthalmic and dermatic applications in these patients, they had completely recovered respectively in 2 to 4 days.

5. Hematological Findings (Table 4)

The hematological changes were observed and comparisons made of the findings as of before treatments and those of terminations. As indicated in table 4, 8 dogs in chloromycetin group were used and 17 dogs in aureomycin group for the hematological examinations.

Before treatments anemia and leucocytosis were apparent in severe cases. Especially neutrophiles increased in parallel to leucocyte numbers and eosinophiles showed a remarkable decrease or disappearance. These hematological findings were gradually altered to normal conditions in parallel with the advance of the treatments in cured cases. The variations of neutrophiles and eosinophiles have important signification in observing the severity of diseases or knowing their prognosis.

TABLE 4. *Hematological Findings*

Gr.	Termin.	Case Nos.	Time of Examination	Eryth. (Mill.)	Leuco. (Thous.)	Percentage in Leucocytes							
						Neut.							
						Met.	Rod.	Seg.	Total	Ly.	Mon.	Eos.	Bas.
Chloromycetin	Recover	5	Before treatm.	495.4	13.2	1.0	12.9	58.7	72.6	6.9	10.1	0.5	—
			Termin.	591.6	12.5	1.7	15.4	53.2	70.3	14.1	13.6	1.7	—
	Death	3	Before treatm.	296.3	21.1	—	4.8	70.0	74.8	14.0	8.1	—	—
			Termin.	381.0	27.2	—	7.3	80.7	87.7	5.5	7.1	—	—
Aureomycin	Recover	11	Before treatm.	524.3	13.6	—	1.9	58.7	60.6	32.7	3.8	2.8	—
			Termin.	657.5	11.5	—	2.4	55.3	57.7	31.6	4.0	6.5	—
	Death	6	Before treatm.	362.0	14.0	—	4.1	70.7	74.8	23.1	1.8	0.3	—
			Termin.	373.1	15.2	—	1.7	83.7	88.4	4.4	7.2	—	—

TABLE 5. *Bacteriological and Parasitological Findings*

Group	Disease's Type	Case Nos.	Feces (Case Nos.)				Nasal Discharges (Case Nos.)			
			Before Treatment		Terminal Time		Before Treatment		Terminal Time	
			C	P	C	P	C	P	C	P
Chloromycetin	Resp.	7	6+(1*)	3+	6+(1*)	2+	1+	—	—	—
			1−	4−	1−	5−	6−			
	Nerv.	6	6+(1**)	3+	6+(1**)		2+	2+	1+	1+
				3−			4−	4−	5−	5−
	Digest.	2	2**+	1+	1*+	2+(1*)	—	—	—	—
				1−	1−					
Aureomycin	Resp.	8	8+(2*)	2+	8+(2*)	3+	1+	—	—	—
				6−		3−	7−			
	Nerv.	8	6+(1*)	1+	8+(1*)	4+	—	—	—	—
			2−	7−		4+				
	Digest.	4	4+	1+	2+	2+	1+	—	1+	—
				3−	2−	2−	3−		3−	

Note: C (*E. coli*), P (*Proteus*), * (*Toxocara canis*), ** (*Dipylidium caninum*).

6. Bacteriological and Parasitological Findings (Table 5)

There being suspicions of secondary infections by *Salmonella* group in gastroenteritis, bacteriological investigations were made on the feces of all dogs. As indicated in table 5, there were found in high degree coli and proteus groups by direct and enrichment cultures in the before and after treatments. On the similar examinations performed on the nasal discharges both these microorganisms were found, but they were much less than in the feces. *Salmonella* group could not be found at all.

In the parasitological findings for the feces of all dogs, parasitic eggs of *Toxocara canis* in 5 and of *Dipylidium caninum* in 1 were found. Each of the hosts of these parasitic eggs was severely affected with gastroenteritis.

7. Pathological Findings

In autopsy findings of 5 corpses in nervous type there were obtained following pathological changes: Catarrhal pneumonia and dilatation of ventricles in 5 respectively; gastroenteritis, anemia of whole body, congestion of spinal cord and interstitial nephritis in 3 respectively; acute myocarditis, catarrahl cystitis and fatty degeneration of liver respectively in 1.

Discussion

From the above presented data, clinical trials with chloromycetin or aureomycin against the patients except for the nervous type have demonstrated the effectiveness of these antibiotics. Several symptoms found in the materials used were considered due to the secondary infections.

Ferry[3,4] and other workers[8,21] reported *Al. bronchisepticus* to be the most frequently isolated organism, further they stated that species of streptococci, staphylococci and even *E. coli* or *S. enteritidis* were found. Recently Hsiung et al. stated that *Micr. pyogenes* var. *albus* and species of streptococci were the commonest organisms found in serous and mucopurulent ocular discharges from dogs affected with distemper.

In the present biological studies, before treatments and terminations for feces and nasal discharges, there were found coli and proteus groups, but other microorganisms were not found. The results of the present examinations are considered to be influenced by the methods of cultures. It will be thought from the data that chloromycetin and aureomycin were not very effective for 2 of the groups found in the present classifications.

Fourteen nervous patients showed marked symptomatic epilepsia and encepha-

litic signs. From many years ago, it has been accepted that if nervous symptoms appear in canine distemper there are on therapeutic agents and the mortality is high. Therapeutic methods in nervous distemper have not been discovered up to date.

On the other hand, it is said that many of the viruses are susceptible to these antibiotics,[19,20,22] but they do not appear to be effective in infections where the viruses are very small. REAGAN and BRUCKNER reported that the distemper viruses are round and have a mean diameter of 21 mμ by direct measurment of electron micrographs. On the basis of their study it may be impossible to inhibit the activity of the distemper virus by chloromycetin and aureomycin.

SUMMARY

The workers tried to make therapeutic experiments in complicated canine distemper with oral administration of chloromycetin and aureomycin. The results thus obtained may be summarized as follows.

1. Chloromycetin was an effective agent in controlling the secondary pneumonia and gastroenteritis of canine distemper. It was administered at the rate of 25 to 50 mg/kg with a mean of 30.3 mg/kg of body weight in divided doses to 4 times per day for 2 to 5 days.

2. Aureomycin was also an effective agent for the secondary invaders in canine distemper as was chloromycetin. The dosage schedules ranged from 25 to 50 mg/kg with a mean of 31.3 mg/kg of body weight divided into 4 times per day for 2 to 5 days.

3. Chloromycetin and aureomycin have no effectiveness for the nervous type of canine distemper insofar as shown in the present experiments.

4. Topical use of aureomycin ointment 1 or 2 times per day for 2 to 4 days has a dramatic value for conjunctivitis and pustular dermatitis accompanying canine distemper.

5. For the treatments in complicated canine distemper, there is needed also symptomatic therapies.

6. By MÜLLER and S. S. media in feces and nasal discharges there were found coli and proteus groups which seemed to have no pathogens; other microorganisms were not found. Researches on the secondary invaders using other cultures are now in progress in our clinic.

7. Varieties of hematological findings, especially in neutrophiles and eosinophiles, have important significance in observing the severity of diseases and to make prongnoses.

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