**NOTE** *Internal Medicine*

# Chloramphenicol Treatment for Rabbit Syphilis

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ABSTRACT. Penicillin, the recommended treatment for rabbit syphilis, sometimes induces adverse effects. The efficacy of oral chloramphenicol was evaluated in 39 cases of rabbit syphilis to establish a safe and efficient treatment for this disease in companion rabbits. All cases clinically improved and recovered promptly. Fourteen of 39 cases (35.9%) relapsed, but most remained chloramphenicol sensitive. Since safety take priority over efficacy in treating syphilis in companion rabbits, chloramphenicol should be chosen as a first- line agent, as a general rule. Three-week administration of chloramphenicol may be adequate at the initial onset of disease. When relapse occurs repeatedly or the rabbit owner cannot administer the medicine adequately, treatment with penicillin should be considered.
KEY WORDS: antibiotic, rabbit syphilis, relapse.

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Recently, veterinary clinicians in Japan have encountered cases of rabbit syphilis caused by *Treponema paraluiscuniculi* [17]. *T. paraluiscuniculi* is sensitive to some antibiotics, similar to *T. palidum*, the pathogenic organism in human syphilis [5, 6, 10, 15, 16, 19]. Penicillin (PC) is commonly used to treat human syphilis [2, 3, 7], except in PC allergic individuals [1], but antibiotic use is more strictly limited in rabbits, due to frequent adverse effects [8, 9, 12, 14, 20]. PC has been shown to be most effective against *T. paraluiscuniculi* infection in laboratory and commercial rabbits [5, 6]. Therefore, PC is recommended as the first choice for treating syphilis in household rabbits [4, 13, 14, 19], but caution is indicated when administering PC to rabbits [4, 8, 12, 20].

To reduce adverse events during the treatment of syphilis in companion rabbits, chloramphenicol (CP) was evaluated in 39 cases of rabbit syphilis at our clinic. The outcomes of CP therapy were analyzed retrospectively to establish safe and efficient treatment for companion rabbits with syphilis.

Forty-eight cases of rabbit syphilis were diagnosed and treated in animals visiting the Saito Rabbit Clinic (Kita-ku, Tokyo) from September 1999 to August 2002. Outcomes were followed up in 39 of 48 cases. Seventeen rabbits (43.6%) were males and 22 (56.4%) were females (Table 1). The age of the rabbits at initial onset ranged from 3 to 39 months, with an average age of 8 months and a median age of 7 months (Table 1). All the rabbits were under 20 months of age, with one exception (No. 14) which was 39 months old (Table 1). 28 of 39 were mongrel rabbits (71.8%), with other breeds including Netherland dwarf (7 rabbits, 17.9%), Holland lop (2, 5.1%), Lion (1, 2.6%), and Rex (1, 2.6%) (Table 1). Body weight ranged from 0.72 kg to 2.56 kg, with an average of 1.46 kg (Table 1). All 24 cases examined were serologically positive for rapid plasma reagin (RPR) test, measured by the RPR Test KOKUSAI (International Reagents Corporation, Kobe, Japan) [18] (Table 1).

Rabbits were treated with CP (Pediatric Chloromycetin® Palmitate, Sankyo, Tokyo, Japan) (55 mg/kg BID p.o.). The dosing period was varied from one to six weeks (Table 1). Twenty-five of 39 rabbits completely recovered after receiving CP, with no relapses for at least a year (No. 1–25) (64.1%). These rabbits received oral CP twice daily for two to six weeks (average of 3.6 weeks). Conversely, relapses were seen in 14 rabbits (No. 26–39), with a relapse rate of 35.9% (14 of 39). These rabbits received CP for one to five weeks (average 3.1 weeks) after disease onset. The relationship between duration of treatment from disease onset and outcome in these 39 cases is shown in Fig.1.

Table 2 shows treatment and months to relapse in 14 rabbits (No. 26–39). Three rabbits relapsed twice and two relapsed three times. Although most cases were treated with CP and recovered clinically, three cases were eventually treated with long-acting PC (Duopen®, Schering-Plough Animal Health) (3 times at weekly intervals, 84,000 IU/kg, i.m.). No cases treated with PC experienced a relapse for at least 8 months. Although 2 out of 3 cases treated with PC showed loss of appetite and activity with and without diarrhea for 2 to 5 days, both cases recovered without treatment. The intervals from the last symptoms to relapse ranged from 2 to 17 months (Table 2).

Although PC is effective, it sometimes causes adverse effects in rabbits [4, 8, 12, 20]. Oral PC administration has also been suggested to be dangerous for rabbits, with parenteral administration safer [5]. Moreover, rabbits should only be fed with hay for several days before PC injection to protect against digestive system disturbance [4]. Incidentally, antibiotics can cause digestive system disturbance and enterotoxemia leading to death in rabbits [8, 9, 12].

Conversely, the risk of adverse effects with CP is negligible [12]. Although 2 of 39 cases showed decreased appetite and activity for several days at the beginning of CP administration, this may be secondary to stress from forceful oral administration. Rabbits should be handled carefully, since they are easily stressed [11]. Forced oral administration of any medication usually causes decreased appetite and activity.

Table 1. Signalment, RPR test result, length of CP[a] administration, and outcome

| No. | Sex | Age (month) | Breed | Body weight (kg) | RPR test | CP[a] administration length (weeks) | Outcome |
|---|---|---|---|---|---|---|---|
| 1 | ♀ | 6 | M[b] | 1.5 | NT[g] | 4 | NR[I] |
| 2 | ♀ | 10 | M | 1.9 | NT | 5 | NR |
| 3 | ♀ | 3 | M | 1.0 | NT | 2 | NR |
| 4 | ♀ | 3 | L[c] | 0.7 | NT | 3 | NR |
| 5 | ♀ | 8 | M | 1.6 | NT | 3 | NR |
| 6 | ♀ | 3 | N[d] | 0.9 | NT | 5 | NR |
| 7 | ♂ | 5 | N | 1.2 | NT | 4 | NR |
| 8 | ♂ | 10 | M | 1.9 | NT | 3 | NR |
| 9 | ♂ | 3 | M | 0.8 | NT | 3 | NR |
| 10 | ♀ | 13 | H[e] | 2.5 | NT | 4 | NR |
| 11 | ♀ | 14 | M | 2.6 | NT | 2 | NR |
| 12 | ♀ | 17 | M | 2.1 | +[h] | 6 | NR |
| 13 | ♀ | 16 | M | 2.0 | + | 2 | NR |
| 14 | ♂ | 39 | M | 1.9 | + | 5 | NR |
| 15 | ♂ | 4 | M | 1.4 | + | 5 | NR |
| 16 | ♀ | 8 | M | 1.6 | + | 3 | NR |
| 17 | ♂ | 7 | M | 1.7 | + | 3 | NR |
| 18 | ♀ | 7 | N | 1.2 | + | 4 | NR |
| 19 | ♀ | 7 | M | 1.7 | + | 2 | NR |
| 20 | ♀ | 19 | N | 1.1 | + | 4 | NR |
| 21 | ♀ | 7 | M | 1.5 | + | 3 | NR |
| 22 | ♀ | 7 | R[f] | 2.4 | + | 3 | NR |
| 23 | ♂ | 8 | H | 1.2 | + | 3 | NR |
| 24 | ♂ | 7 | M | 0.8 | + | 3 | NR |
| 25 | ♂ | 6 | M | 1.3 | + | 5 | NR |
| 26 | ♂ | 6 | M | 1.3 | NT | 2 | R[j] |
| 27 | ♂ | 5 | M | 1.1 | NT | 2 | R |
| 28 | ♀ | 8 | M | 2.0 | NT | 3 | R |
| 29 | ♂ | 5 | M | 1.2 | NT | 2 | R |
| 30 | ♂ | 6 | N | 1.1 | NT | 4 | R |
| 31 | ♀ | 4 | M | 1.0 | + | 3 | R |
| 32 | ♂ | 12 | M | 1.7 | + | 2 | R |
| 33 | ♀ | 7 | M | 1.5 | + | 4 | R |
| 34 | ♂ | 3 | M | 0.9 | + | 5 | R |
| 35 | ♀ | 7 | M | 1.7 | + | 3 | R |
| 36 | ♀ | 15 | N | 2.1 | + | 1 | R |
| 37 | ♀ | 4 | N | 0.8 | + | 4 | R |
| 38 | ♂ | 6 | M | 1.3 | + | 4 | R |
| 39 | ♂ | 6 | M | 1.3 | + | 5 | R |

a) Chloramphenicol b) Mongrel c) Lion d) Netherland dwarf e) Holland lop f) Rex g) Not tested h) Positive in RPR test i) Not relapsed j) Relapsed

The rabbits not experiencing relapse received medication for an average of 3.6 weeks. The rabbits that did later relapse, however, were treated for a shorter period, on average 3.1 weeks. Thus, the duration of CP administration may be related to relapse in rabbit syphilis, but the dosing period is not the only factor, since 4 rabbits received CP for only two weeks without relapse, while 2 rabbits received CP for five weeks and did relapse (Fig. 1).

CP should be given for more than three weeks, since cases treated for more than three weeks showed a lower probability of relapse (30%) than those treated for less than two weeks (55.6%) (Fig. 1), but cases treated for more than four weeks did not necessarily show a lower probability of relapse. Since almost all cases treated with CP showed dramatic improvement within a week, the relapse rate may be

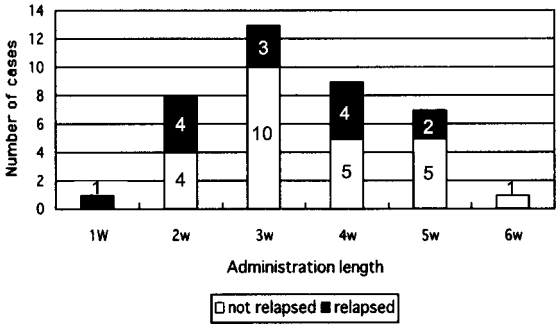


Fig. 1. Relationship between the length of chloramphenicol administration and outcome. Cases that later relapsed are indicated by shaded bars and those that did not relapse are shown as unshaded bars.

Table 2. Treatment and months to relapse in 14 cases of relapse

| No. | Treatment at the initial onset | Months to relapse | Treatment at the 2nd onset | Months to relapse | Treatment at the 3rd onset | Months to relapse | Treatment at the 4th onset |
|---|---|---|---|---|---|---|---|
| 26 | CP[a)]2w[b)] | 5 | CP 4w | | | | |
| 28 | CP 3w | 6 | CP 3w | | | | |
| 30 | CP 4w | 10 | CP 6w | | | | |
| 31 | CP 3w | 17 | CP 5w | | | | |
| 33 | CP 4w | 4 | CP 6w | | | | |
| 35 | CP 3w | 5 | CP 3w | | | | |
| 36 | CP 1w | 8 | CP 2w | | | | |
| 34 | CP 5w | 7 | PC[c)] | | | | |
| 38 | CP 4w | 5 | PC | | | | |
| 39 | CP 5w | 5 | CP 5w | 5 | CP 6w | | |
| 37 | CP 4w | 10 | CP 4w | 4 | CP 6w | | |
| 27 | CP 2w | 2 | CP 4w | 8 | CP 3w | | |
| 32 | CP 2w | 6 | CP 2w | 5 | CP 2w | 5 | CP 2w |
| 29 | CP 2w | 5 | CP 3w | 2 | CP 4w | 8 | PC |

a) Chloramphenicol b) Weeks c) Penicillin

high as a result of the shortened dosing period. Generally, three weeks of CP administration may be adequate at the initial onset of symptoms.

Five of 14 rabbits experiencing relapse had owners who complained of difficulty with medication administration, but only one of 25 non-relapsed cases had similar problems. These six rabbit owners attempted regular administration during the indicated period and clinical recoveries were achieved. Nevertheless, inadequate administration could account for the observed relapses, since the cases with difficult medication administration were more apt to relapse. Rabbit syphilis tends to occur in young animals, as all the cases were observed in animals under 39 months of age (Table 1). Relapse may also be influenced by age. In fact, the 39-month-old rabbit (No.14) did not relapse (Table 1) and rabbit No.32 did not relapse after the last onset at 28 months of age (Table 2).

Proper instruction in oral CP administration may be necessary, since it can be difficult with some rabbits. Rabbit owners should also be instructed to continue therapy for at least 3 weeks, even though clinical signs disappear within a few days of initiating treatment. Intervals from the last appearance of symptoms to relapse ranged from two to 17 months, with a median of five months and a relapse rate of 35.9%. Thus, before dispensing CP, owners should be made aware of the possibility of relapse.

Weekly injection of long acting PC is an easy and reliably effective treatment for rabbit syphilis. Multiple factors must be considered when deciding on anti-microbial therapy. If safety takes priority over efficacy, CP should be selected as the first-line agent. When relapse is seen repeatedly or rabbit owners cannot administer CP adequately, PC i.m. may be considered after a large amount of hay intake and informed consent [4, 8]. When PC is undesirable, CP should be used repeatedly even though relapse can occur several times. Further studies are needed to define the optimal CP dosage.

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