to streptomycin that occurs during subcultures in its presence. None of these 4 antibiotics show any cross-resistance with any of the other antibiotics that are now generally available.

These findings of complete cross-resistance among chemically closely related antibiotics are similar to those shown for the 3 tetracycline analogues(4) and for antibiotics of the erythromycin-group(5). In the latter, complete cross-resistance was found *in vitro* among erythromycin, carbomycin, oleandomycin and spiramycin, but cross-resistance between each of these antibiotics and streptogramin (Antibiotic 900) resembled closely that shown between streptomycin and each of the other 3 antibiotics in the present study.

Summary and conclusions. The antibiotics kanamycin, paromomycin and neomycin were shown to have essentially the same activity *in vitro* against strains of *Staphylococcus aureus* and of various Enterobacteriaceae. Bacteria made resistant to any one of these 3 antibiotics by subcultures on that antibiotic also exhibit virtually complete cross-resistance to the other two. Organisms isolated from infected sources do not show significant cross-resistance between streptomycin and any of these 3 antibiotics. However, strains made resistant *in vitro* to either kanamycin, paromomycin or neomycin show moderate increases in resistance to streptomycin, and strains made resistant to the latter exhibit only minor increases in resistance to the other 3 antibiotics. With all 4 antibiotics, corresponding parent and resistant variants of the staphylococci were of the same phage type, and resistant variants of *K. pneumoniae* and *E. coli* retained their serological specificity. Fecal organisms isolated from patients during oral treatment with paromomycin or kanamycin were resistant to the antibiotic administered and showed moderate to marked resistance also to the other one and to neomycin.

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Experimental Tick Paralysis in Laboratory Animals and Native Montana Rodents. (24335)

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Rapidly engorging females of the Rocky Mountain wood tick, *Dermacentor andersoni,* are a well-known cause of the sometimes fatal tick paralysis of man and some animals in parts of western United States and Canada. Abbott(1) has provided a good clinical and epidemiological review of this disease in various parts of the world. During the years when vaccine against spotted fever was being made from suspensions of infected adult *D. andersoni* at the Rocky Mountain Laboratory, millions of ticks in various stages, including wild-caught adults, were fed on rabbits and guinea pigs. However, so many female ticks have completed engorgement for basic vaccine

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stock and in various investigations with only rare, isolated instances of recognizable paralysis in hosts that systematic attempts to produce this condition experimentally were not attempted until recently.

Flaccid paralysis, uncomplicated by infection, has been seen sporadically in perhaps a dozen rabbits and possibly in a few more guinea pigs. Tick paralysis was suspected in 1938 when partially fed ticks that killed one guinea pig in 6 days also killed, in rapid succession within 24 hours each, 2 others to which the unreplete females were transferred; no animal had gross lesions indicative of intercurrent infection, and blood and tissues of the first produced no growth in bacteriologic media. Previously, a pup on which 3 pairs of laboratory stock ticks were feeding, incidental to another study, developed progressive ascending paralysis over a period of 3 days. Movement of eyes and slow respiration in the prostrate animal were the only actions observed when the female ticks finally completed engorgement. The dog fully recovered 2 days later.

Progeny of ticks in both above instances, as well as those of a few partially fed ticks from human patients, that had not been damaged and were fed and mated on laboratory animals, did not produce disease in test animals either by feeding or when injected. The success reported in British Columbia by Gregson(2), in each of 10 woodchucks (*Marmota*) and 3 ground squirrels (*Citellus*) on which one to several wild-caught *D. andersoni* females were fed, prompted reinvestigation of small animal hosts for susceptibility.

Methods. Adaptations of the usual procedure for feeding ticks on animals in capsule bandages(3) were followed. Wild-caught, adult ticks tested were from British Columbia and the Bitterroot Valley in western Montana. Studies were facilitated through the senior author's discovery that hamsters became paralyzed when bitten by F_1 adult progeny of B.C. ticks which had produced the disease in dogs. Partial to complete paralysis in affected animals was readily diagnosed clinically. Culture in bacteriologic media and transfer of blood and tissues from various affected animals to fresh animals were repeatedly done without demonstrating any infectious agent. This finding was substantiated by absence of significant gross lesions at necropsies.

Results. Paralysis following attachment of 2 to 6 pairs of B.C. ticks to each of 11 local marmots (*M. flaviventris*) and 15 ground squirrels (*C. columbianus*), in addition to hamsters, has confirmed Gregson's observations. Unexpectedly, however, 11 of 18 guinea pigs (approximately 200 g) died on the 7th and 8th days after attachment on each of 4 pairs of B.C. ticks and with illness of less than 10 hours; one of 6 which were bitten by Bitterroot ticks died on the 10th day. So far, B.C. ticks have completed engorgement on 7 white rats, 5 rabbits, and 6 cats (part of these ticks included partially fed ones transferred from paralyzed hamsters) without producing disease. On the other hand, 3 young wood rats (*Neotoma cinerea*) died in 4 to 7 days after attachment of 4 pairs of B.C. ticks on each.

Results of current tests with various animals (Table I) reveal that even in hamsters not all ticks caused paralysis, but that the highest percentage of transmission was by B.C. ticks. Furthermore, after initial feeding of 4 or more days on fatally affected hamsters, single ticks 1/3 or more engorged have produced death in as few as 12 hours after reattachment to fresh hamsters. Death in a guinea pig within 21 hours was caused by reattachment of 2 half-fed ticks from a fatally affected hamster. B.C. and Bitterroot males alone, either initially fed on or transferred from paralyzed hamsters, caused no paralysis during prolonged attachments on young hamsters. Suspensions of salivary glands from engorged, innocuous females and from fed males produced at most temporary uneasiness in dogs and hamsters when injected intraperitoneally. Many animals from which ticks were removed early in illness have fully recovered, usually within a few to 24 hours.

Illness begins with a short period of hyperactivity followed by incoordination of locomotion. In a few hours progressive flaccidity develops, followed by inability to raise the head. The hind limbs of woodchucks frequently show spastic rigidity. In almost all

TABLE I. Summary of Tests of *Dermacentor andersoni* to Produce Tick Paralysis in Different Small Animals.

No. ♀ ticks originally fed on each host	Animal hosts	No. used	No. positive	Days until onset	No. died	Remarks*
Brit. Columbia						
(Wild) †						
2– 4	Hamsters	57	22	4– 6	10	12 recovered
1	"	33	17	4– 7	7	7 " ; 3 spontaneous
1– 3	White rats	7	0	0	0	Incl. 3 sucklings
4– 6	Guinea pigs	18	11	5– 8	11	
1– 2	" "	15	5	½–10	5	Part-fed ticks transferred from paralyzed hamsters
4	Ground squirrels	15	13	1– 7	13	
4– 6	Woodchucks	11	11	5– 9	8	3 recovered
4	Wood rats	3	3	4– 7	3	
4–14	Dogs	11	7	6–11	3	4 "
4	Cats	6	0			
(Progeny) †						
1–6	Hamsters	79	34	4– 8	22	10 " ; 2 spontaneous
6	Rhesus monkey	1	1	8		Recovered
(Both)						
2–8	Rabbits	5	0			Incl. 3 weanlings
Western Montana						
(Wild)						
4–5	Hamsters	54	18	4– 6	14	4 recovered
4	Guinea pigs	6	1	10	1	
(From 3 human cases)						
1	Dogs	2	0			3 part-fed ♀ ticks completed feeding
	Hamster	1	0			

*"Recovery" in each instance followed early removal of ticks; 5 additional listed as "spontaneous" recovered while ticks still attached.

† "Wild" refers to adult, unfed ticks captured in nature; "progeny," to adult ticks reared in the laboratory.

hamsters, the eyes become closed with a copious conjunctival exudate, a condition which was observed in only 2 ground squirrels of the other animals tested. A rapid drop in temperature, respiration, and pulse is noted as illness progresses. In woodchucks temperature has reached as low as 28°C for 24 to 48 hours with a concomitant respiration rate of only 7 per minute. In affected dogs and a monkey, knee jerk was absent during the episode. Heart beat was usually strong for some time after respiratory failure. The only gross lesions observed at necropsy were hyperemic congestion of lungs with some excess pleural fluid and a suggestion of inflammation of small intestine.

In most instances, the disease was fatal to small animals tested when ticks were about half or even less engorged. Four times, however, hamsters recovered spontaneously when single female ticks apparently were slowed in their engorgement, and one hamster recovered after complete flaccidity while 4 females were still feeding. In 2 dogs and a monkey, ticks which were feeding unusually slowly caused only partial paralysis and incoordination of the legs over a period of several days. Lack of fertilization unquestionably slowed feeding of some female ticks.

Following are sample series of early tests with numbered hamsters infested with adult progeny of B.C. ticks previously engorged on paralyzed dogs:

Line A. 8 pairs of ticks on No. 18; flaccid paralysis 8 a.m. day 5, dead before noon; ticks removed 9 a.m. *First transfer:* 2 pairs each to Nos. 21-24; Nos. 21 and 22 developed flaccid paralysis in 27 hours, No. 23 in 39 hours; all 3 resumed full activity 6 to 13 hours after removal of ticks; No. 24, ticks completed feeding in 2½ days, no effect. *Second transfer:* 2 ticks from No. 21 reattached

to a guinea pig, animal dead in 21 hours; one tick from No. 22 to No. 29, animal dead in 23 hours.

Line B. 6 pairs of ticks on No. 19; flaccid paralysis 8 a.m. day 5, dead before noon; ticks removed 9 a.m. *First transfer:* 2 pairs to each of Nos. 25-27; flaccid paralysis, No. 25 in 54 hours (sacrificed when moribund), No. 26 in 18 hours (recovered 7 hours after removal of ticks), No. 27 in 11 hours (dead 2 hours later). *Second transfer:* Ticks from Nos. 26 and 27 completed engorgement on 2 young beagle dogs in 2 to 3 days, no effect.

Another series with wild-caught B.C. ticks illustrates susceptibility of hamsters recovered up to 67 days after original severe attacks:

Hamster 202 (recovered 45 days) developed typical signs 5 days after 4 pairs of ticks attached, but again recovered after early transfer of ticks to No. 260. Latter (recovered 28 days) paralyzed in 24 hours; again recovered after early transfer of ticks to No. 123. Last (recovered 67 days) became paralyzed in 10 hours but was fully recovered after ticks had finished feeding in less than 24 hours.

Hamsters have also been used to test our laboratory tick stocks of *D. andersoni, D. variabilis, Rhipicephalus sanguineus* (Egyptian strain), as well as wild-caught *D. occidentalis* from Oregon, without becoming paralyzed, though 3 of 10 tests of *R. sanguineus* were equivocal.

Conclusions. It is hoped that a means has now been provided, through use of hamsters, to study more intensively the incitant of this disease and to determine its possible relationship to the toxic principle reported by Steinhaus(4) in *D. andersoni* eggs. Ecologic and/or genetic factors may be influential, but it is pertinent that reared progeny of paralysis-producing ticks have now induced experimental disease. In spite of successful transmission by partially fed ticks from paralyzed animals in many of the above experiments, individual female ticks that produced paralysis in 3 child patients of Drs. Barmeyer and Adlerson of Missoula completed engorgement and mated on 2 dogs and 1 hamster, respectively, in 2 to 4 days without reproducing paralytic signs in these hosts. These observations indicate that hamsters are the animals of choice for the study of tick paralysis.

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Polydipsia and Polyuria During Chronic Administration of Levorphanol to Rats.* (24336)

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This paper is a report of preliminary experiments on observations of polydipsia and polyuria in rats treated chronically with levorphanol (Levo-Dromoran Tartrate). Interest in these observations arises from the fact that effects described are in apparent direct antithesis to the generally reported antidiuretic action of levorphanol. Also, close chemical and pharmacological similarity of levorphanol with morphine indicates that these observations may be of pertinence in relation to the action of morphine.

Materials and methods. To measure water intake and urine excretion, rats were placed in individual metabolism cages. The metallic funnel shaped floor of cage was coated with

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