ingeal infections produced by susceptible organisms, without the need of supplementary intrathecal therapy. Inasmuch as the concentration of penicillin at comparable periods varies with different subjects, it would appear, however, that larger and/or more frequent doses than have generally been administered intravenously or intramuscularly may be required to obtain the maximum bacteriostatic effects and to preclude the development of penicillin resistance. Whether this method of therapy will be as effective or produce clinical responses as promptly as that observed when combined with intrathecal administration (Rosenberg and Arling)[6,7] must await clinical trial. Further studies along this line are indicated.

SUMMARY AND CONCLUSIONS

(1) Penicillin was administered in doses of 20,000–40,000 Oxford units intravenously or intramuscularly to 8 subjects with meningitis. Sixty to 140 minutes later penicillin was found in the spinal fluid in concentrations of 0.03 to 0.35 unit per cc.

(2) These data suggest that penicillin administered intravenously or intramuscularly in adequate dosages may be effective in the treatment of meningitis without supplementary intrathecal therapy.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

THE GOLDEN HAMSTER (CRICETUS AURATUS) AS A TEST ANIMAL FOR THE DIAGNOSIS OF LEPTOSPIROSIS

THE investigation of leptospirosis due to infection with *Leptospira canicola* has been seriously handicapped by the lack of a readily susceptible laboratory host, whereas numerous species are known to be susceptible to *L. icterohaemorrhagiae*.[1]

Meyer, Stewart-Anderson and Eddie[2] chose young guinea pigs weighing 50–100 grams for their studies on canine leptospirosis. They state that the spirochetes associated with dog infections are of a low pathogenicity for rodents and that in young guinea pigs weight loss was a better criterion of infection than a febrile reaction. However, three to five passages were required to produce a definite weight loss and an occasional fatal infection.

The purpose of this paper is to report the use of hamsters for the isolation of both *L. canicola* and *L. icterohaemorrhagiae* from naturally infected dogs, and further, to report the first instance in which the classical strain, *L. icterohaemorrhagiae,* has been isolated from the dog in the United States.

SUSCEPTIBILITY OF HAMSTERS TO VIRULENT STRAINS OF LEPTOSPIRA

Our early attempts to isolate Leptospira from the blood and urine of dogs following the injection of suitable material into young guinea pigs were as unsatisfactory as those reported by Meyer and his co-workers.[2] The experimental data on the use of hamsters reported by Morton[1] and the suggestion of Dr. Carl L. Larson, of the U. S. Public Health Service, led to the choice of hamsters three to four weeks old and weighing 25 to 30 grams for experimental work.

Leptospira canicola was first isolated in young hamsters after injection of the urine of an acutely ill dog whose serum on the day the urine sample was collected had a positive agglutination titer for *L. canicola* in a dilution of 1–2,000 and a cross titer for *L. icterohaemorrhagiae* in a 1–10 dilution. The urine specimen was obtained by catheter on February 15, 1943, and centrifuged in an angle centrifuge at 3,500 RPM for one-half hour. The sediment was suspended in sterile saline solution and injected intraperitoneally into four young hamsters and four young guinea pigs. Within 9 to 10 days the hamsters died of leptospirosis. *L. canicola* was demonstrated by dark-field examination of portions of the kidney and liver, in sections stained by a silver staining method and cultured in Fletcher's broth. The injected guinea pigs remained normal in appearance.

This strain of *L. canicola* isolated from dog urine injected in young hamsters has been labelled Strain "A" and the confirmation of its pathogenicity for hamsters has been reported by Larson[3] in his paper on "Experimental Leptospirosis in Hamsters." On the second passage of this strain in hamsters marked icterus appeared three to four days after injection of the animals, death following within 5 to 6 days after inoculation.

Later the owner of the dog from which Strain "A" was isolated became seriously ill with canicola fever, the diagnosis being based on the serologic findings and the demonstration of leptospira in his urine by dark-

[6] D. H. Rosenberg and P. A. Arling, *U. S. Naval Med. Bull.* In press.
[7] *Ibid.: Jour. Am. Med. Assoc.* In press.
[1] H. E. Morton, *Proc. Soc. Exp. Biol. and Med.*, 49: 566, 1942.
[2] K. F. Meyer, B. Stewart-Anderson and B. Eddie, *Jour. Am. Vet. Med. Asn.*, 95: 710, 1939.
[3] C. L. Larson, Public Health Reports, 59: 522, 1944.

field examination. At this time no hamsters were available and urine specimens prepared as described above failed to infect young guinea pigs.

L. canicola Strain "B" was also isolated after the intraperitoneal injection of young hamsters with urine sediment from a dog ill with leptospirosis. This dog of the Boxer type apparently became ill on June 15, 1943. The owner, who became ill and was hospitalized on July 25th, admitted having removed soiled newspapers from the dog's quarters on July 4th. The medical officer in charge of the patient reported that her serum developed an agglutination titer of 1–1,000 for *L. canicola* and a cross agglutination titer of 1–10 for *L. icterohaemorrhagiae.*

On August 10th serum obtained from the dog gave a positive agglutination reaction for *L. canicola* in a dilution of 1–1,000 and a cross agglutination for *L. icterohaemorrhagiae* in a dilution of 1–10. At the same time a urine specimen was obtained by catheterizing the dog. The resuspended sediment prepared as previously described was injected into four young hamsters and four young guinea pigs. On August 22 one of the hamsters died and from its kidneys and liver *L. canicola* was cultured in Fletcher's broth and leptospira demonstrated on tissue section.

Isolation of L. Icterohaemorrhagiae from a Dog

On May 26, 1943, a Boston terrier was brought to the dispensary presenting symptoms of leptospirosis. A sample of venous blood was obtained and injected intraperitoneally into two young hamsters which died 6 and 7 days after injection. (From this time attempts to infect guinea pigs was abandoned because of our inability to establish an infection, whereas infections were regularly produced in the hamster.)

Leptospira were observed by the dark-field examination of fresh kidney and liver material, in stained sections, and were cultured in Fletcher's broth.

On May 8th a urine specimen, prepared as previously described, was obtained from this dog and injected into four hamsters, three of which died within 2 to 3 days from bacterial infection. The fourth hamster died of leptospirosis eight days after injection. Marked icterus was evident at the time of death. Leptospira were observed by dark-field examination, in tissue sections, and cultured in Fletcher's broth. Typing of the recovered organism from the blood and urine proved it to be *L. icterohaemorrhagiae.*

This dog had a history of having caught rats in a chicken house on the owner's property. The symptoms manifested in this animal were quite mild in comparison with those in the previously mentioned two dogs ill with *L. canicola* infection. This is the first isolation of *L. icterohaemorrhagiae* from a dog in the United States, previous diagnoses of infection with this species of leptospira having been based on serologic findings.

Differential diagnosis of *L. canicola* and *L. icterohaemorrhagiae* infections may be achieved by injecting material from the suspect into both young guinea pigs and young hamsters, since only the hamster will succumb to infection with *L. canicola* while *L. icterohaemorrhagiae* infections terminate fatally in both species.

Summary

There is evidence that the golden hamster (*Cricetus auratus*) is the animal of choice for the isolation of leptospirae, especially of the *Leptospira canicola* type since young guinea pigs and mice are resistant to infection and rats are entirely refractory. Both the classical strain, *L. icterohaemorrhagiae* and *L. canicola* on isolation have been found to produce a fatal infection in hamsters.

The present report deals with the isolation of *L. canicola* in two instances by the injection intraperitoneally into hamsters of urine obtained from dogs ill with suspected leptospirosis. Each of the dogs was apparently the source of infection for a human case of *Canicola leptospirosis.*

The classical strain *L. icterohaemorrhagiae* was isolated from the dog for the first time in the United States. In this instance the organism was isolated by injecting both whole blood and urine from the patient intraperitoneally into young hamsters.

The injection into hamsters of suitable material from patients infected with *L. canicola* and *L. icterohaemorrhagiae* is followed by a fatal leptospirosis in the test animal.

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