10750 P

Periodicity of Sporadic Bacillemia in Experimental Tuberculosis in Dogs.

JOHN S. HOWE. (Introduced by A. J. Nedzel.)

From the Department of Pathology, Bacteriology and Public Health, University of Illinois, College of Medicine, Chicago, Illinois.

The author[1] has reported the occurrence of sporadic bacillemia in 17 of 20 dogs infected experimentally with virulent human tubercle bacilli (H 37). This report represents a further study of some factors in the time relationships of bacillemia in tuberculous dogs, including some of the animals included in the previous report.

Dogs were injected intravenously or subcutaneously with virulent human tubercle bacilli (H 37) in a suspension of Kaolan, mineral oil, and normal saline, the doses ranging from 3 to 20 mg. Femoral arterial punctures were performed daily on all dogs, and 3 to 5 cc of arterial blood withdrawn, under sterile precautions and injected directly into guinea pigs, usually subcutaneously in the right inguinal region. Endermal tuberculin tests were done on all guinea pigs before inoculation with the dogs' blood, and at intervals up to 3 months after inoculation, when all were sacrificed and necropsied.

The presence of tuberculosis was established on the basis of the characteristic pathology of injection—tuberculosis, supported by positive tuberculin reactions and microscopic examination of smears for tubercle bacilli.

All guinea pigs injected on 2 successive days were usually kept in the same cage during the 3-month period of observation. At necropsy it was noted that in some cages there was a high percentage of guinea pigs positive for tuberculosis while in other cages all were negative. The possibility that this might be due to spontaneous infection was considered. However, as Saenz *et al.*[2] have pointed out, spontaneous laboratory infection does not occur in less than 6 months' exposure, and the longest period of exposure to infection possible in this experiment was 3 months. Moreover, the anatomical distribution of the tuberculous lesions in our guinea pigs conformed closely to those described by Wilson[3] as typical of in-

1 Howe, J. S., PROC. SOC. EXP. BIOL. AND MED., 1939, **40**, 509.

2 Saenz, M., Costil, L., and Sadettin, M., *Compt. rend. Soc. de Biol.*, 1935, **119**, 266.

3 Wilson, *Tuberculous Bacillemia*, London, 1933.

jection—tuberculosis *i. c.*, inguinal glands and spleen chiefly involved, rarely liver, very rarely lungs or intestines.

From these considerations it seemed that spontaneous infection could be excluded. Furthermore the possibility that errors in technic might play a part seemed unlikely, since the blood was drawn daily under sterile conditions and injected directly into guinea pigs which were then carefully identified and segregated.

Since technical errors and spontaneous infection could be eliminated as causes, this apparent periodicity of bacillemia in animals observed at the same period seemed to justify further study.

Charts were made for each dog showing the occurrence and relative amount of bacillemia on each day of the observations. Charts of all dogs observed over the same period of time were then superimposed to show any periods of bacillemia occurring in several or all of the dogs. Protocols for 3 such periods of observation, representing the major part of the experiment, are appended.

These protocols confirm the tendency to periodicity of bacillemia in dogs observed over the same period of time. This periodicity seems not dependent on the duration of the infection, for it is evident in animals inoculated at different times but observed during the same experiment. It seems to be unrelated to the outcome of the infection, for it is evident in comparing the charts for animals that recovered with those that died. It seems independent of the anatomical distribution of the tuberculous lesions, as is evident in comparing the charts of dogs injected intravenously with those injected subcutaneously.

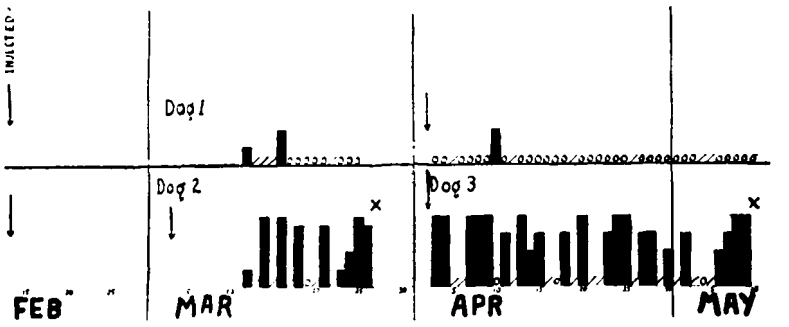

FIG. 1.

Each small square represents one day. Day of inoculation is indicated by arrow. Solid black columns denote bacillemia, the height of column roughly indicating the degree of bacillemia. Negative days indicated by 0. Diagonal line represents days on which no blood was drawn.

Dog No. 1 was injected subcutaneously. Dogs 2 and 3 were injected intravenously. Note the close correspondence of periods of bacillemia.

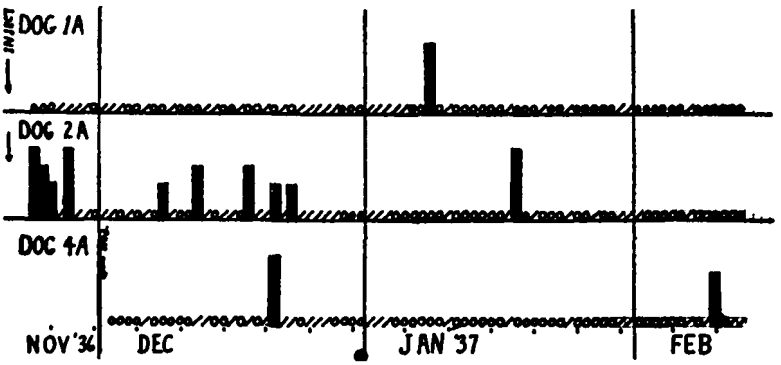

FIG. 2.

Dogs 1A and 2A injected intravenously. Dog 4A injected subcutaneously. Less marked similarity of charts, but 2A and 4A correspond on December 21st.

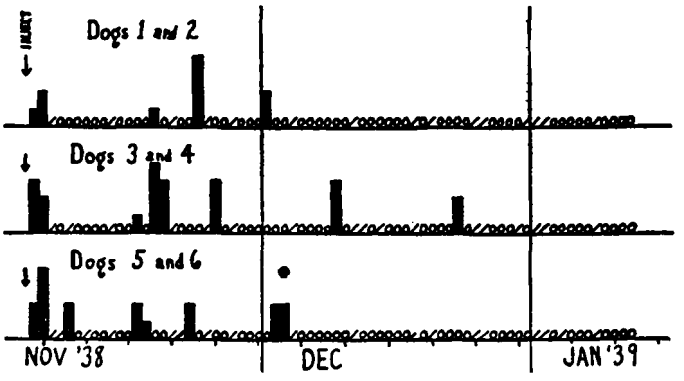

FIG. 3.

All dogs injected intravenously. Blood from each pair of dogs (1 and 2, etc.) pooled before injection. Periods of bacillemia are strikingly similar in the three groups of dogs.

Search of the literature reveals no mention of periodicity in bacillemia, although certain clinical findings might well suggest the possibility. The explanation of this periodic bacillemia, simultaneous or closely following in several dogs, must lie in some factor which tends to affect all the animals in the same manner at about the same time. All dogs were on standard diets and under good laboratory conditions. Further study of various environmental factors in relation to this periodic bacillemia is in progress.