acid-soluble phosphate as well as the 7-minute hydrolyzable and residual phosphates. A marked rise in liver glycogen and considerable improvement of the clinical status of the animals was also noted. It is important to emphasize that enormous doses, up to 60 units of insulin, were necessary to bring about these improvements in comatose rats. It will be seen that although the degree of the response was not uniform the trends are definite.

SUMMARY

Alloxan given parenterally produces in the rat a state of diabetic coma which is analogous to the severe coma of human diabetes. Such animals, moreover, show a rise in plasma inorganic phosphate and blood sugar. They also show in the liver a decrease in glycogen and in the total acid-soluble phosphates. An increase in liver inorganic phosphate occurs with a concurrent fall in adenosine pyrophosphate and other organo-phosphates. Hence the rise in plasma inorganic phosphate during coma is at least partially due to a loss of liver phosphate. It is probable that this rise in plasma inorganic phosphate results from a breakdown of organo-phosphates which result from the depressed oxidations associated with insulin lack. Insulin, when administered in exceptionally large doses, tends to cause improvement in both the clinical and chemical state of comatose rats.

NATHAN O. KAPLAN
MAURICE FRANKS
CHARLES E. FRIEDGOOD

DEPARTMENTS OF MEDICINE AND ANATOMY,
WAYNE UNIVERSITY COLLEGE OF MEDICINE,
DETROIT

AN EPIZOOTIC OF PNEUMOCOCCUS TYPE 19 INFECTIONS IN GUINEA PIGS[1]

OUTBREAKS of pneumococcal infections among guinea pigs have been known for some time to occur in this country and in Europe.[2] The epidemic strains and the pneumococci found in normal guinea pigs have not usually been classified serologically and those that were fell into the so-called Group IV. In 1932, Neufeld and Etinger-Tulczynska[3] identified the type 19 pneumococcus as the prevalent type in both healthy and infected guinea pigs of various laboratories and dealers in Berlin and elsewhere in Germany. At that time Webster could not find this organism in the nasal washings of guinea pigs in New York.[3] To our knowledge carriers of type 19 pneumococci or spontaneous infections with this organism have not been described among guinea pigs in the United States.[4]

The infections reported in this paper occurred among apparently healthy guinea pigs in the course of studies of certain effects of sodium salicylate in these animals. The occurrence of unexpected deaths among experimental and control animals prompted a bacteriological study which revealed that the type 19 pneumococcus was the cause of most of the fatal lesions. In addition, carriers of the same organism were found among apparently healthy guinea pigs. Sulfadiazine was used prophylactically in one group of animals in an attempt to eliminate the infections and to clear the carrier state.

Materials and Methods. The 3 groups of guinea pigs used in this study were procured from different dealers in widely separated localities. They were apparently healthy when received and no infections had previously been recognized in the stock from which they came. Nasal washings were obtained for culture in the first group as soon as the epizootic was recognized. In the other 2 groups they were done when the animals were first observed. These cultures were repeated at autopsy and, in addition, cultures were made from swabbings of the cut surfaces of the lungs, of the internal ears, nasal accessory sinuses and other purulent foci at that time. The nasal washings were done as described by Neufeld,[2] saline being used for the washings in the first group and broth in the other groups. The cultural methods for isolation and identification of the pneumococci were those described elsewhere.[1] Autopsies were done as soon as possible after the death of the animals or immediately after they were sacrificed (by stunning). Flamed instruments were used to cut the lungs and to open the bony structures before taking the cultures. The organs were examined grossly and also microscopically from Zenker's-fixed, paraffin sections stained with hematoxylin-eosin. The sodium salicylate and the sulfadiazine were fed to the animals by stomach tube, a separate tube being used for each animal. Their diets were not otherwise controlled. Cultures of the rabbit chow used to feed the animals yielded no pneumococci. The observations in each of the 3 groups will be presented separately.

Group I. The 20 guinea pigs in this group were delivered to the animal quarters at the Harvard Medical School on February 5, 1945, from a breeder in Saugus, Mass., which is about 10 miles north of Boston. After a few days they were brought to the animal house of the Neurological Unit at the Boston City Hospital, where they were kept thereafter in a

[1] From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital and the Department of Medicine, Harvard Medical School, Boston, Mass.

[2] For a review of the epidemiology of pneumococcal infections in animals see M. Finland, *Medicine*, 21: 307, 1942.

[3] F. Neufeld and R. Etinger-Tulczynska, *Ztschr. f. Hyg. u. Infektionkr.*, 114: 324, 1932.

[4] In 1938, Geoffrey Rake (*Am. J. Hyg.*, 28: 377) described spontaneous infections due to *S. enteritidis*, type 19 pneumococcus and *A. bronchosepticus* in a guinea pig breeding colony at the farm division of the Connaught Laboratories in Toronto.

single cage. As part of an experiment, 10 of these animals were given daily feedings of sodium salicylate by stomach tube and the others were being kept as normal controls.

A few days after the experiment was started, 6 of the treated animals died in rapid succession and large hemorrhagic areas were found in their lungs. These were thought at the time to be due to aspiration of the intubated material. Shortly thereafter, 3 control animals died and had similar pulmonary lesions. The possibility of an epizootic was then considered and cultures were made from the lungs of the next animal that died. These yielded type 19 pneumococci in almost pure culture.

Nasal washings of the 10 surviving animals were then cultured and the same organism was identified in only one of them. None of these animals showed any evidence of illness at this time and they were still kept in the same cage. Deaths occurred in 4 more animals from 5 to 9 days later and the same type of pulmonary lesion was found in each instance. In addition, one of them had bilateral purulent otitis and pleuritis and also pericarditis and another had pericarditis and multiple pulmonary abscesses. The only manifestations of illness in any of the animals were apathy and anorexia for 2 days before death. When the last of these animals died, the 6 survivors were sacrificed, but only 1 of them showed any significant pulmonary lesions. Type 19 pneumococci were found from one or more cultures in all but one of the animals that died and from 4 of 6 that were sacrificed. They were grown from the lungs of 4, the ears and sinuses of 6, the pleural exudates of 1 and the blood of 1. Many other organisms, notably gram positive and gram negative bacilli, staphylococci and indifferent streptococci were also found but were not considered to be significant.

Group II. On April 9, 1945, 4 days after the preceding experiment was terminated, 20 guinea pigs were received at the animal quarters of the Harvard Medical School from a dealer in Canton, Mass., which is about 15 miles south of Boston. Nasal washings from these animals were made and cultured on the following day and type 19 pneumococci were obtained from 4 of them. The guinea pigs were all brought to the same animal house at the Boston City Hospital, where the carriers were isolated and the remaining guinea pigs were kept together in a single large cage in a different room from the one previously used. All the animals appeared to be in perfect health.

The previous studies with sodium salicylate were repeated and, in addition, both the treated and control animals were given daily doses of sulfadiazine by stomach tube in an attempt to prevent and control the infections. A separate tube was used for each animal. Satisfactory sulfadiazine blood levels were maintained. Cardiac blood taken 24 hours after a dose showed levels ranging between 5.4 and 9.5 mgm of free drug per 100 ml. In spite of these precautions 2 animals died, one after 14 and the other after 20 days. Neither of them originally had positive nasal cultures. Type 19 pneumococci were obtained from cultures of the lungs and nasal washings at autopsy in one, but this organism could not be recovered from the other; although the latter had pneumonia of one lobe. The remaining animals were all sacrificed between the fifteenth and twenty-second days. Bronchitis, peribronchitis and focal bronchopneumonia were found in 4 of these animals.

Type 19 pneumococci were found at autopsy in 9 animals. They were found in nasal washings in 6, in the lungs of 3 and in the nasal accessory sinuses in all 9 of them. Among the 4 original carriers, it was found at autopsy in the nasal washings and sinuses of one and from the latter site alone in another.

Group III. This group consisted of 16 guinea pigs which were delivered on May 4, 1945, directly to the animal rooms of the Thorndike Memorial Laboratory from a breeder in Lenox, Mass., about 135 miles west of Boston. The animal rooms were in a different building from those of the Neurological Unit and were in charge of a different attendant. The animals were apparently in good health and showed no external evidence of infection. Nasal washings were done with broth soon after these animals arrived. These were cultured and inoculated into mice. Type 19 pneumococci were obtained from cultures of 7 of these animals and in 2 of them these organisms were grown in almost pure culture.

Summary and Conclusions

An outbreak of respiratory infections among guinea pigs occurring in the late winter and early spring of 1945 is described. The type 19 pneumococcus was identified as the organism responsible for the fatal lesions. The same organism was found in the respiratory tract of other apparently healthy guinea pigs obtained from three breeders in widely separated localities in Massachusetts. Although the type 19 pneumococcus has previously been found to be widespread in healthy and infected guinea pigs in Germany, this is probably the first time this organism has been identified under similar conditions in the United States. Sulfadiazine appeared to control the infections, in part, but did not eliminate the carrier state.

F. Homburger
Clare Wilcox
Mildred W. Barnes
Maxwell Finland