not affected. The rate of apposition is accelerated in the enamel-covered portion and decelerated in the cementum-covered portion. The findings indicate the delicate response of the rate of dentin apposition to Vitamin-A deficiency and suggest the possible use of this reaction as a biologic method of measuring the Vitamin-A content of foods.

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A Pneumonia-Producing Filtrable Agent from Stock Mice.*

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A virus causing respiratory disease in stock mice has been reported by Dochez, Mills and Mulliken.[1] We have encountered a similar infectious agent, have made a preliminary pathological study of it, and have attempted to compare it with the Dochez virus and with other agents of disease found in stock mice. The chief purpose of this report, however, is to call attention to the ease with which the disease caused by this agent may be confused in mice with infection due to influenza virus.

Pharyngeal washings from patients with a variety of illnesses (common cold, atypical pneumonia, influenza-like illness) were inoculated intranasally into mice which were sacrificed on the sixth day. The lungs were removed aseptically, emulsified, and passed intranasally to normal mice which were in turn sacrificed, the series being continued indefinitely. As controls, serial passages were made from mice inoculated intranasally with pharyngeal washings from normal persons, with broth, and with normal mouse lungs. In every instance, after a varying number of transfers, lung lesions resembling those produced by influenza virus began to appear in the mice. Their initial appearance varied from the first to the ninth passage and they became maximum in 2 or 3 further passages, killing the mice usually on the third or fourth day. White mice purchased in the open market and weighing 5 to 10 g have been used exclusively, and lung

* This work was supported in part by a grant from the Fenger Memorial Fund.

1 Dochez, A. R., Mills, K. C., and Mulliken, B., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 683.

lesions have appeared in mice from 2 different dealers. The appearance of the mice before death and the macroscopic appearance of the lung lesions were the same in all mice, irrespective of original source of inoculum, indicating that the infectious agent was present in the stock mice.

The first signs of illness in the mice are a ruffled coat, a hunched posture and a decrease in food consumption. As the infection progresses, their movements become sluggish, respiration may be labored, and they finally become moribund and die. No mice have survived when once their appearance indicated that infection had occurred. Examination of mice sacrificed at various intervals after inoculation shows that the lungs are first involved at the apices and the dorsal portions. The affected parts are sharply demarcated from the remaining normal lung and have a greyish-pink color. The infection then extends to involve practically all lung tissue and at death the lungs are of a uniform dark red color.

The microscopic lesion in the lungs is characterized by diffuse interstitial pneumonia consisting almost entirely of mononuclear leukocytes and an occasional polymorphonuclear cell. The distribution is generally patchy, but the patches become confluent. The bronchiolar epithelium is well preserved and the lumens occasionally contain exudate composed of mononuclear and polymorphonuclear leukocytes. Although the pneumonic changes are practically identical with those produced by influenza virus in mice, the characteristic desquamation and metaplastic replacement of the bronchiolar epithelium seen in influenza[2] is absent in this diesase. In the liver, focal necrosis of the hepatic cells occurs without other significant inflammatory changes. This further differentiates the disease from influenza in which the liver is usually undisturbed. The infectious agent is present in livers of infected mice as demonstrated by intranasal inoculation.

Blood agar plate cultures have been made routinely of lung emulsions used for inoculation. During the first passages such cultures incubated aerobically and anaerobically almost uniformly showed no growth. Since then bacterial growth has occurred oftener and is due perhaps to a noticeable decrease in the quality of the stock mice used. Lung emulsions have also been cultured upon chocolate agar plates and in brain broth tubes. All types of bacteria found upon these media and anaerobic blood agar plates also grew upon aerobic blood agar plates. When growth does occur it may consist of gram negative rods, gram negative diplococci, or alpha hemolytic

2 Straub, M., *J. Path. and Bact.*, 1937, **45**, 75.

streptococci. Mixed cultures are the rule. The type of organisms and amount of growth appear to be totally unrelated, however, to the presence and severity of the lung infection. Mixtures of the cultivated bacteria have not produced illness in mice following intranasal inoculation. Because of the apparent lack of association with cultivable bacteria filtration tests were made. Berkefeld N filtrates of dilute broth emulsions of lungs have caused the infection in 5 of 9 attempts, Seitz filtrates in 1 of 3 attempts. In each case the filtration was controlled by addition of an emulsion of *Bact. prodigiosum* to the material to be filtered. No filtrates showed growth.

After the first observations on this infectious agent had been made it was noted that a previous report by Dochez and his colleagues[1] described an infection which appeared to be quite similar to the one we have encountered. Through the courtesy of Dr. Dochez we were able to inoculate mice with lung tissue from their mice. The results obtained were not different clinically or pathologically from those seen in mice infected with our agent. Although the mice showed severe lung lesions at the first passage and the series was carried through 9 generations, it cannot be stated with certainty whether the Dochez virus was passed or the infectious agent of our stock mice was again encountered. Since convalescent mice are not available and production of an antiserum has been unsuccessful to date, cross-immunity tests have not been possible.

Thus far we have not been able to identify the infection described here with any other of the diseases of stock mice. Intracerebral inoculation of mice, and intracerebral, intranasal and subcutaneous inoculation of guinea pigs has caused no apparent illness, indicating that the virus of acute meningo-pneumonitis[3] and of lymphocytic choriomeningitis are not present. We have never seen the characteristic features of infectious catarrh[4] in our mice and have not found the coccobacillary bodies associated with this disease in emulsions of infected lungs. The apparent independence of this infection from cultivable bacteria indicates it is not due to the *Bacterium influenzæ murium*.[5] Mice have been inoculated intraperitoneally and into the foot pads with lung emulsions without producing apparent disease. Such mice showed no resistance to a subsequent intraperitoneal inoculation of ectromelia virus.

Because of the marked resemblance of this infection to that produced by influenza virus in mice we have attempted to make as close

3 Francis, Thos., Jr., and Magill, T. P., *J. Exp. Med.*, 1938, **68**, 147.

4 Nelson, John B., *J. Exp. Med.*, 1937, **65**, 833; *ibid.*, 843.

5 Kairies, A., and Schwartzer, K., *Zentralbl. f. Bakt.*, 1936, **137**, 351.

a comparison of the two as possible. Four mice, 1 month convalescent from influenza virus (Chicago strains), were inoculated intranasally with a regular passage emulsion of our infected mouse lungs. There was no evidence of any immunity to the infection. Similar tests with influenza virus in influenza convalescent mice have shown a definite immunity. The converse cross-immunity test has not been done due to lack of convalescent mice. No evidence of *in vitro* neutralization was found using antiserum prepared in the rabbit against the PR 8 strain of human influenza virus. Three human serums (patients supplying original pharyngeal washings) also gave no neutralization.

The present significance of this infection appears to be the possibility of its confusion with influenza virus infection in mice or its interference with other work in which mouse lungs are passed. Slight clinical and microscopical differences may be noted between this infection and that of influenza virus, but in general they are quite similar. Our own experience will illustrate the possible difficulties which may arise. After several months' storage in glycerin, 4 strains of human influenza virus were passed rapidly through 4 generations of mice by intranasal inoculation of lung emulsions. A serum neutralization test was done, using a serum which had previously shown strong neutralizing properties against human influenza. No neutralization occurred in any strain, and our conclusion was that our influenza virus had become contaminated with and possibly replaced by the other agent.

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Neurogenic Fever Reduced by Nembutal.*

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Following operations on the brain in the region of the optic chiasma and infundibulum, patients frequently develop a hyperthermia which is difficult to control and is often fatal. Similar sharp rises in temperature have been obtained in cats and monkeys by placing lesions in the anterior part of the hypothalamus or in the preoptic region. These operations were performed under nembutal anesthesia and the hyperthermia did not appear until the depressing effect

* Aided by a grant from the Rockefeller Foundation.