this work to study quantitatively the potency of morphine in this respect, but these preliminary data reveal that morphine produces urine with about 0.6 times the antidiuretic potency of 1.5 milli-units of pitressin/100 g body weight (tested in a similar manner). Moreover, the absence of this effect of morphine when injected into hypophysectomized rats strengthens the hypothesis that the origin of the antidiuretic substance found in the urine of normal rats receiving morphine is the neurohypophysis.

Table 2 demonstrates the effects of various physical and chemical treatments on the antidiuretic activity of urine from rats receiving morphine. It is clear that all the treatments, with the exception of the sodium sulfite, destroyed the antidiuretic substance just as they are reported to destroy the antidiuretic hormone (*5, 6*). In the case of the sodium sulfite, one experiment showed complete inactivation, and two experiments revealed only partial inactivation. Gilman and Goodman have reported a similar inconsistency in their experiments on the influence of sodium sulfite on the activity of the antidiuretic hormone (*6, 7*).

We feel that these preliminary data support the view that morphine stimulates the production of an antidiuretic substance by the neurohypophysis; and, further, that this substance has properties markedly similar to those reported for the antidiuretic hormone. A more detailed qualitative and quantitative characterization of this substance is being undertaken.

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An Outbreak of Mouse-Pox (Infectious Ectromelia) in the United States: I. Presumptive Diagnosis[1]

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During the summer of 1951 an epizootic disease made its appearance for the first time in the mouse colonies of the Department of Anatomy of Yale University School of Medicine. Infected mice usually appeared in good health until a few hours or a day before death, at which time the fur became ruffled, with a characteristic puffy appearance about the face. The most constant autopsy findings were a pale, mottled liver, hemorrhagic appearance of the proximal inch or two of the small intestine, pulmonary congestion or consolidation, and hemorrhagic appearance of the base of the claws. Death of one mouse in a pen was usually followed by death of all or most of the other mice in that pen, with similar autopsy findings, over a period of a few days or a few weeks. All attempts to prevent the spread of the disease from pen to pen were futile.

At the end of 6–8 weeks the disease had spread to practically all pens of mice. Combined mortality of all the colonies of the department often exceeded 100 mice/day. In approximately 4 months after onset, the death rate had returned to a normal level. Although exact figures are not available, it is estimated that at the end of this period the total mouse population had been reduced to approximately 50% of its initial size. Of the animals alive at the end of this time, many had been born during the course of the epizootic. Of the animals existing at the onset of the disease, therefore, less than 50% survived. The mortality rate appeared to be higher among some strains (A and BC) than among others (C_{57}). One group of over 100 mice of the A strain, set aside for a particular experiment, suffered 100% mortality.

While the death rate was still increasing, foot pad inoculations were undertaken because of the similarity of some of the findings to those described by Dingle (*1*) for the acute phase of infectious ectromelia. At the time no cutaneous lesions were apparent. Liver suspensions from 5 mice believed to have the disease were injected into the foot pads of healthy mice. Four of the 5 suspensions proved infectious. The injected foot of all 18 mice receiving these 4 suspensions became inflamed and edematous, usually on the third day. Fourteen mice died, and 3 were killed when death seemed imminent, in from 4 to 7 days (av, 5.2). Smears of the injected foot failed to reveal bacteria. Autopsy findings were similar to those described above for the spontaneous disease. The eighteenth mouse survived; its injected foot became edematous, exudative, scabbed, and underwent progressive loss of the distal half, suggestive of the chronic cutaneous phase of infectious ectromelia. Several weeks later, after the death rate in the colony had returned to a low level, cutaneous lesions of the tail, feet, face, and body appeared spontaneously in many of the surviving mice.

The chlorioallantoic membrane of chick embryos was inoculated with a suspension of liver from one of the 18 experimentally infected mice. Autopsy findings on this mouse were typical of the spontaneous disease. Eight of 12 inoculated eggs showed pocklike lesions of the membrane, similar to those described by Burnet (*2, 3*) for the virus of infectious ectromelia. Seven of these membranes were pooled, ground, and centrifuged. The supernatant suspension was injected into the foot pads of 7 mice. Six died on the sixth day and one on the seventh day, with swollen foot pad and autopsy findings similar to those of the spon-

[1] This investigation has been aided by grants from the Jane Coffin Childs Memorial Fund for Medical Research and the U. S. Public Health Service.

taneous disease. Of 10 mice inoculated with material from the second egg generation (after intervening lyophilization), 4 died on the fifth day and 6 on the sixth day, with swollen foot pad and autopsy findings similar to those of the spontaneous disease. This culture has been carried through 6 egg generations, with intervening storage in glycerol. Penicillin and streptomycin have been added since the third egg generation. It has continued to reproduce the same proliferative pocklike lesion of the chick membrane, and the same disease in mice not previously exposed.

Intracytoplasmic, eosinophilic inclusion bodies have been observed in tissues from both infected mice and eggs. They were, however, not as frequently found in the tissues of infected mice as might have been expected from the literature on infectious ectromelia. Moreover, because of their lack of specificity, definitive diagnosis should depend not on the presence or absence of inclusion bodies, but on serological or immunological methods.

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An Outbreak of Mouse-Pox (Infectious Ectromelia) in the United States: II. Definitive Diagnosis[1]

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The immunological similarity of the viruses of infectious ectromelia and vaccinia was first reported by Burnet (*1–3*) on the basis of the following observations:

a) The virus of infectious ectromelia, growing on the chick chorioallantois, produces a soluble hemagglutinin which agglutinates the same spectrum of fowl erythrocytes agglutinated by vaccinia hemagglutinin.

b) Both ectromelia and vaccinia hemagglutinins are inhibited by either ectromelia or vaccinia immune sera, but not by normal sera.

c) Vaccinia can be used to immunize mice effectively against ectromelia.

On this basis Burnet suggested that infectious ectromelia is the murine representative of the mammalian pox diseases, and proposed (*4*) that the term "mouse-pox" should be used as a synonym for infectious ectromelia. This work has been confirmed and considerably extended by Fenner (*5–11*), who adopted "mouse-pox" to describe the disease, but retained "ectromelia" to describe the causative virus.

Definitive diagnosis of the disease described in the preceding article (*12*) was made by demonstration of vaccinia antihemagglutinin in the sera of convalescent mice, and by successful cross-immunization with vaccinia against the isolated etiological agent.

Approximately 2 months after the mortality rate had returned to normal, 18 mice that had lived through the epizootic were bled and the sera tested for inhibition of the hemagglutinin produced by the Nelson and Levaditi strains of vaccinia virus. Six of the sera inhibited 4 agglutinating doses of vaccinia hemagglutinin at dilutions of 1–20 to 1–80. Nine of the sera showed no inhibition of vaccinia hemagglutinin at a dilution of 1–10. At the same time 14 sera from a group of mice separated from the main colony during the course of the epizootic, but before showing manifestations of the disease, were tested. One showed inhibition of vaccinia hemagglutinin at a dilution of 1–48. The remaining 13 were negative at a dilution of 1–6.

TABLE 1

CROSS-IMMUNIZATION BY VACCINIA (NELSON) AGAINST THE ISOLATED ETIOLOGICAL AGENT

Intranasal vaccinia	No. of mice	Specific mortality following foot pad inoculation 19 days later
None	30	20/30
1–100 Dilution	29	6/29
1–5 Dilution	29	3/29

For cross-immunization, mice were used from a source without previous known exposure to either vaccinia or ectromelia. Two groups received intranasal inoculation, under ether anesthesia, of vaccinia (Nelson) at dilutions of 1–5 and 1–100. A third group received no vaccinia. Nineteen days later all three groups were challenged by foot pad inoculation of the etiological agent, isolated as previously described (*12*). Those groups exposed to vaccinia showed definite protection (Table 1). The experiment was repeated, using a different strain of vaccinia (Levaditi) and a 40-day interval between intranasal inoculation and foot pad injection. The mice receiving vaccinia were again protected (Table 2).

Mouse-pox is enzootic in laboratory mice in Europe. The U. S. has been remarkably free of the disease. Importation of the virus is prohibited by the U. S. Bureau of Animal Industry (*11*). Serological surveys for the presence of vaccinia antihemagglutinin in mice from different breeding stocks in the neighborhood of New York City and Boston failed to reveal a single positive result (*11*).

Fenner (*11*) quotes two references (*13, 14*) and a personal communication (*15*) suggesting that the disease may previously have existed in the U. S. The

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