results obtained with our inhibitor-sensitive strains do indicate that the difficulty of removing their erythrocyte receptors with neuraminidase is due to their position in the receptor gradient. If so, the rate at which they are destroyed by neuraminidase will depend on the concentration of the enzyme as well as the duration of treatment. Variations in either of these factors would explain the discrepancy between our results and those of other authors.

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Latent Ectromelia

ECTROMELIA, a highly infectious disease of mice, is caused by a pox virus closely related to the causal agents of variola and vaccinia. The disease is frequently found in laboratory mice, and its existence poses a difficult problem for those responsible for the supply of laboratory animals. It therefore seems worth while to record certain preliminary observations which may bear on the epidemiology of the disease.

Fenner¹ showed that a large amount of virus was excreted from the skin of mice which developed a rash, and he believed the chief mode of infection was contact of virus with abraded skin². Virus ceased to be excreted 3 weeks after the onset of the rash, and recovered mice were immune to re-infection. The epidemic behaviour and antibody response resembled the pattern associated with smallpox and seemed incompatible with persistent infectiousness of recovered mice. However, the carriage of ectromelia virus in colonies of apparently healthy mice has long been suspected, and accounts have been published of the appearance of acute ectromelia following the inoculation of mice with various biological substances³⁻⁵. The authors interpreted their observations in terms of the hypothesis that the virus may be carried in latent form in apparently normal mice.

In the hope of resolving these differences, attempts were made to isolate the virus from mice which had survived infection with small doses inoculated intraperitoneally. Although the virus was not isolated from cultured spleens later than 37 days after inoculation and most recovered mice appeared healthy, a few developed regressive lesions on the tails quite insignificant compared with those produced by the inoculation of the virus into the tails of normal mice. This observation and the observation of Dr. Janet Niven that apparently healthy mice may manifest microscopic lesions characteristic of ectromelia in the intestine led me to look for virus in the tail skin and faeces of recovered mice. Virus was isolated both from the intestinal contents and tail skin of each of six mice 84 days after infection and from the tail

skin of 2 of 5 mice 99 days after infection⁶. These results indicated that virus is excreted into the intestine and from the tail skin of recovered mice long after the development of immunity and clinical recovery. Such mice could presumably infect the next generation of mice and infection of each successive generation might follow.

Experiments are being undertaken to investigate whether ectromelia can be transmitted from generation to generation in this way, and some facts of interest have come to light, although these experiments are still incomplete. It appears that mice can be regularly infected *per os* with large doses of virus (10^6 LD₅₀ or more, as measured by intraperitoneal inoculation of mice) and that even with much smaller doses of virus *per os* ($<10^3$ LD₅₀) about 1:5 mice are infected. Oral infections, unlike infections following intraperitoneal and footpad inoculation, are often inapparent with large doses of virus and practically always so with small doses. Such inapparent infections may be recognized by the development within 3-4 weeks of immunity to withstand intraperitoneal inoculation of 10^6 LD₅₀ of virus and by isolation of virus from the tails and intestinal contents. Thus, two mice died of 120 (2 per cent) infected *per os* with doses ranging from 10^3 to 10^4 LD₅₀, while 20/88 (23 per cent) of these became immune. Twenty-seven mice died of 59 (46 per cent) after 10^6 or more LD₅₀ of virus *per os* and 27/31 (87 per cent) of the survivors were immune. Virus was isolated in mice from the tail skin and faeces of one mouse of seven given *per os* 10^2 LD₅₀ of virus 81 days before. Virus was similarly isolated from the tail skin and/or faeces of mice infected *per os* with large doses (10^6 LD₅₀ or more) as shown in Table 1.

Table 1	
Days after oral infection	Ratio: Mice which yielded virus Mice examined for virus
32-35	2/9
69	3/8
81	2/4
116	1/4
	8/25 (32%)

These results show that ectromelia can be an inapparent infection and that mice may harbour the virus in the intestinal tract and tail skin for a long time. The possibility of a similar situation with other diseases of the pox group deserves consideration. Virus was isolated more frequently from the tail skin than the faeces. Nevertheless, it seems likely that faeces are the principal source of virus and that the tail skin becomes infected by faecal contamination. The presence of antibody in the faeces would explain the fewer virus isolations from this source. Isolations of virus have been attempted only from individual mice, but experiments are now being undertaken to determine whether virus can be isolated from tail skin or faecal suspensions of groups of mice. This might provide a simple screening test for ectromelia in colonies of mice, to supplement the usual test for haemagglutination-inhibiting antibodies.

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