

## **Innate resistance to myxomatosis in wild rabbits in England\***

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### SUMMARY

Wild rabbits (*Oryctolagus cuniculus*) from one study area in England have been used over a period of 11 years to investigate the possible appearance of innate resistance to myxomatosis. Rabbits of 4–6 weeks old were captured alive, retained in the laboratory until at least 4 months old, and then infected with a type of myxoma virus which kills 90–95% of laboratory rabbits. Observations were made of symptoms, mortality rate and survival times.

In the first 4 years of the study (1966–9), mortality rates were not significantly different from those of laboratory rabbits, although survival times of wild rabbits were appreciably longer. In 1970, the mortality rate amongst wild rabbits was 59%, in 1974 it was 17%, and in 1976 it was 20%, thus showing that a considerable degree of inherited resistance to myxomatosis has developed.

The types of myxoma virus most commonly isolated from wild rabbits in Great Britain in recent years have been those which cause 70–95% mortality in laboratory rabbits. Therefore, if the degree of innate resistance demonstrated is widespread in Great Britain, there are serious implications regarding the size of the rabbit population, because myxomatosis has been an important factor in holding rabbit numbers at a relatively low level.

### INTRODUCTION

Myxoma virus evolved in the Americas and is found as a natural infection of certain *Sylvilagus* species, in which it causes a very mild infection that is rarely fatal. In European rabbits (*Oryctolagus*) it produces the disease known as myxomatosis and when first introduced to wild European rabbits in Australia and in Great Britain it proved virtually 100% lethal. Since the first introduction there have been clear indications of an accommodation in the virus-host relationship; the appearance of attenuated types of myxoma virus and the establishment of moderately attenuated types as the most common viruses found in wild rabbit populations (Marshall & Fenner, 1960; Fenner & Chapple, 1965). There is evidence also, from Australia, that several populations of wild rabbits have developed a considerable degree of inherited resistance to myxomatosis (Marshall & Fenner, 1958; Marshall & Douglas, 1961; Douglas & Tighe, 1965). Sobey (1969) has shown that, by selection, a strain of resistant laboratory rabbits can be built up. In

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Britain, rabbits from two areas were investigated from 1964 to 1967 (Vaughan & Vaughan, 1968), but mortality rates were not significantly different from the expected values, though survival times did appear to be lengthening. We report here the results of the continued investigation of rabbits from one of the study areas.

#### METHODS

##### *Study area*

Rabbits were obtained from part of an estate near Downham Market in Norfolk. Myxomatosis first reached the estate in 1954, resulting in a very high mortality. Rabbit numbers increased very slowly at first and then more steadily despite the reappearance of the disease in 1960, and its continuous presence ever since, and parts of the estate have held large numbers of rabbits since the middle 1960s.

##### *Virus*

The Brecon strain of myxoma virus (Chapple & Bowen, 1963) used in 1968 was from the same batch as used previously (Vaughan & Vaughan, 1968). This batch was passaged once in a New Zealand White rabbit and then used in 1969 and 1970; the material from a further passage was used in 1974 and 1976.

Virus preparations were titrated by intradermal injection of series of dilutions on the shaved flanks of laboratory rabbits and the number of rabbit infectious doses (RID 50) were calculated.

For testing of resistance, rabbits were injected intradermally on the shaved flank with 0.1 ml of virus suspension diluted to contain approximately 50 RID 50/0.1 ml.

##### *Rabbits*

In most years, young rabbits (generally 4–6 weeks old) were caught alive in the study area, dusted with pyrethrum powder and transported to the laboratory. In 1970, 1974 and 1975 small numbers of rabbits were bred in captivity from adult stock captured in the study area. All rabbits were held in captivity for at least 3 months, to ensure that any myxoma virus antibodies acquired from immune does would have decayed. They were then bled from the marginal ear vein and sera were tested by the Sobey method of agar gel diffusion (Sobey, Conolly & Adams, 1970) and by serum neutralization test (Vaughan & Vaughan, 1968), and rabbits that possessed detectable titres of myxoma virus antibodies were rejected. The remaining rabbits were injected with virus, as were groups of New Zealand White rabbits used as controls. The onset of symptoms, times of death and numbers of survivors were recorded. Mean survival times were calculated using estimation by moments (Sampford, 1954) in cases where one or more rabbits survived.

#### RESULTS AND DISCUSSION

The results of infection, with the Brecon strain, of rabbits obtained from the study area over the period 1966–76 are shown in Table 1(a), with aggregated results of infection of New Zealand White rabbits. The results for 1966–9 show

Table 1. Tests for 'genetic resistance' in wild rabbits

Virus strain	Year	No. of rabbits tested	No. of survivors	Mortality rate (%)	m.s.t. (days)	Range (days)
(a) Brecon	1966	41	4	90	29.8	19-49
	1967	34	2	94	24.6	18-39
	1968	71	10	86	29.4	16-56
	1969	74	12	84	31.9	13-50
	1970	27	11	59	30.6	15-37
	1974	15	13	13	—*	16 and 19
	1976	63	50	21	—*	25-59
Domestic controls		96	1	99	20.2	14-33
(b) Cornwall	1974	11		100	15.2	12-26
	1975	11		100	18.0	11-25
	Domestic controls	5		100	12.0	11-14

\* m.s.t. not calculated because of large numbers of survivors.

that the mortality rates of wild rabbits were not very different from the mortality expected for that strain of virus (approx. 90%). There is an indication of increases in the mean survival times and the ranges of survival times as suggested by Vaughan & Vaughan (1968).

In 1970, the mortality rate (59%) was significantly lower than in previous years and in 1974 it was even lower (13%), but in both years the numbers of rabbits tested were small. For a number of practical reasons, it was not possible to test rabbits in 1971, 1972 or 1973, and, in 1975, rabbits were injected with Cornwall strain (see below). However, the relatively large number of rabbits which were tested in 1976 showed a similarly reduced mortality rate (21%). The survival times of the 13 rabbits which died, ranged from 25 to 59 days with a mean of 37.5 days – considerably longer than previously recorded. There can be no doubt that the rabbits from the study area now exhibit a significant degree of innate resistance to myxomatosis.

Amongst the 50 rabbits which survived myxomatosis in 1976, there was a wide range of symptoms. Seventeen of the survivors showed the full range of symptoms (eyes completely closed, swollen ear-bases, ano-genital swellings); a further 23 developed conjunctivitis and eye-lid swellings of varying severity; 10 developed only local lesions at the site of injection.

Because of the low mortality of rabbits infected with Brecon strain in 1974, a group of 11 rabbits born in 1974 and a further group of 11 born in 1975 were infected with the Cornwall strain of virus (Fenner & Marshall, 1957). The results (Table 1b) show that the mortality rate was 100% but mean survival times were significantly higher than those of domestic rabbits. The numbers of rabbits used were small but it appears that the innate resistance demonstrated against the moderately attenuated Brecon strain does not protect against the virulent Cornwall strain, though some degree of resistance may be responsible for the increased survival times.

The rabbit population of the study area has been subjected to enzootic myxomatosis with epizootics at least once a year since 1960, and the type of virus

has, in all cases tested, been moderately attenuated (Grade IIIa as defined by Fenner & Marshall, 1957). The rabbits have now been shown to have developed a degree of innate resistance against this type of virus.

The development of resistance to myxomatosis in British wild rabbits is not unexpected, because of the earlier Australian results, and it is an example of one side of the natural accommodation of a virus–host relationship; the other side being the attenuation of the virus (Marshall & Fenner, 1960; Fenner & Chapple, 1965). How quickly and how far this accommodation is likely to go are questions which cannot yet be answered, but our knowledge of the relationship between myxoma virus and *Oryctolagus* over the last 25 years indicate that the process will probably be fairly slow.

In Australia and in Great Britain, moderately attenuated strains of virus quickly became the most common strains found in the field (Marshall & Fenner, 1960; Fenner & Chapple, 1965). It is believed that this state of affairs has continued and that further attenuation has not occurred, because strains of moderate virulence are more efficiently transmitted than strains of higher or lower virulence (Fenner, Day & Woodroffe, 1956; Mead-Briggs & Vaughan, 1975).

Mead-Briggs & Vaughan (1975) found that the efficiency of transmission of myxomatosis by fleas is inversely related to the survival time of the host rabbit. We have observed that, in rabbits which show some resistance to myxomatosis, the survival times of those rabbits which die are considerably longer than those of unselected stock. Combining these findings, it appears likely that, as resistance becomes widespread, the moderately attenuated strains will not be transmitted as efficiently, and ever more virulent strains will replace them as the most common field strains. There may also be mutations giving rise to 'super-virulent' virus strains (cf. Fenner & Marshall, 1957, Glenfield strain), and this process could stabilize the host–virus relationship for some time.

To assess the immediate impact of the development of resistance to myxomatosis, it is necessary to consider the current position in the study area and in many other similar areas throughout the country. There is an annual cycle of rabbit numbers with the peak numbers in summer being perhaps five- to tenfold higher than over-winter numbers. The summer peak is due to the appearance of large numbers of young rabbits, some of which will be temporarily protected from myxomatosis by antibodies acquired from immune does. This temporary immunity lasts only for 1–2 months, and thus there are large numbers of non-immune rabbits in late summer and autumn. Epizootics of myxomatosis occur most commonly at this time of year and the rabbit population is reduced to leave an over-winter population, most of which consists of rabbits which have recovered from the disease and are immune.

However, it has been observed that in the apparent absence of myxomatosis, most of the young rabbits are killed by other causes, e.g. predators, control, other diseases, before or during the winter. From this, we can infer that many of the rabbits killed by myxomatosis would have been killed by some other cause, and that the effect of innate resistance would not be as dramatic as may appear from the decrease in mortality rate in laboratory tests from 90 to 20%. None-

theless, even a very small increase in the percentage of young rabbits surviving into the following breeding season can lead to substantial increases in rabbit numbers in spring and summer, when rabbit damage to crops is likely to occur. If innate resistance to myxomatosis becomes widespread, there will be a need for more and better rabbit control.

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