A review of myxomatosis among rabbits in France

C.P. ARTHUR * and C. LOUZIS **

Summary: Myxomatosis is a poxvirus infection which was introduced into France in 1952, and spread throughout Europe, with major repercussions for populations of both wild and domestic rabbits. Since then, the disease has evolved and diverse epidemiological cycles are reported among wild rabbit populations, linked to interaction between vector populations, rabbits and the level of immunity acquired by these rabbits. Two forms of disease are encountered on rabbit farms. The first form, seen on intensive, enclosed premises, is characterised by an irregular cycle, low morbidity and slight mortality. Transmission is exclusively airborne. It appears that this form operates in a totally autonomous fashion. The second form is seen in traditional types of rabbit husbandry in hutches in the open air or protected by a roof. The clinical picture is similar to that of typical myxomatosis among wild rabbits with higher morbidity and mortality. Coincidence in space and time with outbreaks in wild rabbits leads to the suspicion that a winged vector is responsible for these outbreaks and that this form of domestic disease is the result of sylvatic myxomatosis. In both forms, the application of an adequate vaccination programme prevents outbreaks among domestic rabbits whereas no prophylactic measures have as yet proved efficacious among wild populations.

KEYWORDS: Disease control - Epidemiology - France - Myxomatosis - Oryctolagus cuniculus - Poxviridae - Rabbit diseases - Rabbit farming - Viral diseases - Wild animals.

HISTORY

A poxvirus infection originating on the American continent, myxomatosis was first recognised when domestic rabbits were introduced at the end of the nineteenth century (8). The disease was benign in its original hosts, the American rabbits Sylvilagus brasiliensis and Sylvilagus bachmani, but showed a high mortality rate in the European wild rabbit, Oryctolagus cuniculus. As a result of damage to the environment caused by wild rabbits in many countries, attempts were made at the end of the 1940’s to introduce myxomatosis into Australia, New Zealand, Scotland, Sweden and Denmark. While released locally, the virus did not become implanted in any of these countries. The first successful introduction of the virus occurred in Australia in 1950. In France, Professor Armand-Delille introduced the virus into his
property at Maillebois in Eure-et-Loir on 14 June 1952. Taking into account the results obtained elsewhere, Professor Armand-Delille believed that the epidemic would remain confined to his walled enclosure. Nevertheless, by autumn 1952 outbreaks of myxomatosis had occurred in several Departments of France, and by the end of 1953 the entire country was declared to be infected. The virus reached England in October 1953, Italy and Spain in 1955-56, and all of Europe was affected by the end of the 1950's (11).

IMPACT ON RABBIT POPULATIONS DURING THE 1950'S

The severity of losses inflicted on domestic rabbits at this time is difficult to evaluate. During the 1950's, rabbits were kept by farming families as a complement to other farming activities, and there were few major breeding centres. In 1953, the Fur Federation estimated the annual production of rabbit skins to be between 80 and 100 million units, and the loss due to myxomatosis was estimated at 15-20% in 1953-54. The losses were felt in both skin and meat industries. These figures apply only to large rabbit farms, however, and do not take into account the numerous hutches for domestic use in the countryside and suburbs at that time. In this type of situation, it is probable that the impact was more severe than in intensive enterprises. Among wild rabbit populations, the disease had enormous repercussions, as shown by hunters' bag-records during this period. In 1953-54 hunters reported yields of only about 15% compared to the numbers of rabbits shot before 1952; in 1954-55 the figure dropped to 2% and in 1955-56 about 7%. Losses due to myxomatosis thus represented 90-98% of the wild population in France from 1952-55 (10), and the population remained at a low level until the end of the 1950's despite efforts by hunters to set up sanitary barriers through the use of a heterologous vaccine based on Shope's fibroma virus. Attempts were later made to introduce Australian rabbits, which were presumably resistant to myxomatosis, but this too proved unsuccessful.

IMPORTANCE AND KINETICS OF EPIZOOTICS AMONG WILD AND DOMESTIC RABBITS BETWEEN 1953 AND 1967

The kinetics of epizootics among wild rabbits displays three peaks between 1953-67, namely in 1957, 1960 and 1965. Nonetheless, the number of rabbits affected was generally in decline. More than 100,000 dead animals were reported in 1957 compared to 10,000 in 1960 and 5,000-6,000 in 1965* (Fig. 1) (17). Between 1953-67, the number of domestic rabbits affected reached a peak in 1955, then declined, and from 1960 stabilised at about 10,000 rabbits affected per year (Fig. 2) (17). Each year there was a very pronounced seasonal rhythm with a peak in August-September, and no cases between December and May-June. In some years, such as 1959 (Fig. 3) (17), there were also outbreaks in spring. During the annual peak, some 2,000 outbreaks occurred among domestic rabbits each fortnight. During the epizootic peak, over 1,000 domestic rabbits were affected each fortnight, and on some occasions there were more than

* These statistics represent the number of wild animals found dead and sent to Veterinary Services for examination. The actual number of dead rabbits is obviously far greater.
FIG. 1

Kinetics of myxomatosis epizootics among wild rabbits in France (calculated from the number of dead animals examined by the Veterinary Services 1953-1967) (17)

FIG. 2

Myxomatosis outbreaks among domestic rabbits in France, 1952-1966 (17)
Seasonal rhythm of myxomatosis outbreaks among wild and domestic rabbits in France, 1959-1966 (17)

700 new outbreaks in two months (17). Although the situation among wild rabbits was usually not reported, the seasonal rhythm of outbreaks was largely the same as in the domestic species.

IMPORTANCE AND KINETICS OF EPIZOOTICS AMONG WILD AND DOMESTIC RABBITS BETWEEN 1985 AND 1986

Statistics for myxomatosis in both wild and domestic rabbits in France were not processed after 1967, and only recently has there been a national survey of the situation among domestic rabbits. In comparison with the data for 1953-66, it is obvious that
there has been a considerable fall in the number of cases (less than 100 in 1985-86) (23). The seasonal peak has changed slightly to October-December, with about ten cases each month (Fig. 4) (23). However, it is difficult to obtain through such data an idea of the actual economic impact of myxomatosis, because a large number of breeders no longer declare outbreaks which occur on their premises. Thus P. Duclos (personal communication) found that during 1985-86 no case of myxomatosis was recorded by the relevant services of the Ministry of Agriculture for the Rhone Department, while a survey conducted by the Lyons National Veterinary School revealed a number of outbreaks among domestic rabbits during the same period. According to Poirel (27), in 1983-84 myxomatosis among farmed rabbits represented less than 1% of mortality from all causes, while Mercier (26) claimed that it was still a major problem. In the Rhone Department, Marbach (23) found a low incidence of virus, with 1-4% of premises affected (out of 325 premises visited), involving 2,700 rabbits, 1,950 of which died during 1985-86.

Recent studies of the dynamics of wild rabbit populations in various situations and national surveys have provided a more complete epidemiological picture. On the national scale, 20% of communes are free from myxomatosis, in 15% myxomatosis

\[ \text{FIG. 4} \]

Cases of sylvatic and domestic myxomatosis reported in France from January 1985 to March 1986 (23)
occurred throughout the year, 39% experienced the disease in summer alone, against
12% in spring, 18% in autumn and 8% in winter. The disease is absent from all upland
and mountainous Departments (mean altitude over 500 m), while it is present
throughout the year in Departments with plains along the valleys of major rivers.
Overall, the impact of the virus on wild rabbits was judged to be severe by half of
the hunting associations consulted, while 20% stated that it had little effect, and 8%
claimed that myxomatosis had no effect, even though it was present (1).

Comparison of the present myxomatosis situation in different regions of France,
as revealed by various field surveys, shows considerable differences from the position
existing between 1953 and 1967. Table I summarises the principal characteristics of
regional situations. Whereas in southern France (Vaucluse and Camargue) epizootics
always seem to occur at the same time (in summer in the Camargue and in autumn
in the Vaucluse), in the Paris region epizootics can occur at practically any time of
the year (Fig. 5). In Isère, Gilot et al. (12) found a similar situation, with most

| TABLE I |
| Status of myxomatosis in the Vaucluse, the Camargue and the Paris region |

<table>
<thead>
<tr>
<th></th>
<th>Vaucluse** (n = 3)</th>
<th>Camargue* (n = 5)</th>
<th>Paris region** (n = 9)</th>
</tr>
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<tbody>
<tr>
<td>Average length of epizootic (months)</td>
<td>2.2 ± 0.6 (1.5-3)</td>
<td>3 ± 1 (2.3-5)</td>
<td>3.1 ± 1.9 (1-6)</td>
</tr>
<tr>
<td>Average interval between two epizootics (months)</td>
<td>9.8 ± 0.4 (9.5-10)</td>
<td>9.7 ± 0.6 (9.0-10)</td>
<td>9.4 ± 6.5 (4-24)</td>
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<tr>
<td>Cumulative % of animals affecteda</td>
<td>83 ± 29 (44-100)</td>
<td>59.9 ± 27 (25-100)</td>
<td>41 ± 31 (5-88)</td>
</tr>
<tr>
<td>Estimated % mortalityb</td>
<td>39 ± 10 (31-50)</td>
<td>61 ± 10 (50-68)</td>
<td>54 ± 13 (36-78)</td>
</tr>
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<td>% of losses in the populationc</td>
<td>32 ± 8 (21-43)</td>
<td>36 ± 11 (27-51)</td>
<td>22 ± 20 (3-58)</td>
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<td>No. of epizootics:</td>
<td></td>
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<td>spring</td>
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<td>summer</td>
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<tr>
<td>winter</td>
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<td>4</td>
<td>2</td>
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n = no. of epizootics monitored
* Data from Rogers (29) and Vandewalle (33)
** Data from Arthur (unpublished)
a) Sum total of percentage of infected animals observed monthly
b) Estimated according to the number of cases of acute myxomatosis in relation to the total
   number of cases (including recoveries)
c) Derived by multiplication of a x b

epizootics occurring in late spring and early summer during the three years studied
(Fig. 6) (28). The epizootics last longest in the Paris region: about 4 months against
3 in the Camargue and 2.2 months in the Vaucluse. Moreover, while all three regions
had an identical mean period between epizootics of 9-10 months, the variation was
Seasonal rhythm of outbreaks observed among wild rabbits in three regions of France
(Average monthly percentage of animals with myxomatosis, based on 3-9 years of study)
(Arthur and Vandewalle, unpublished data)
The intensity of an epizootic is greatest in the Vaucluse, for 83% of rabbits may be affected within just two months. However, in all three areas there is considerable variation between years in the proportion of rabbits affected, with the Paris region once again showing the widest variations. The mortality rate caused by the field virus (calculated from the number of acute cases in relation to the total number of cases, including convalescent rabbits) varies according to terrain and year from 38 to 61%. The proportions of rabbits of different age groups affected by myxoma virus also show regional variations (Table II). While very few rabbits weighing under 500 g are affected in the Camargue and Vaucluse,
this age group accounts for approximately 20% of cases in the Paris region. In the
last-named region, about 33% of adults captured show signs of myxomatosis, while
almost no adult is affected in the Camargue and Vaucluse.

Thus it seems that myxomatosis has undergone pronounced regression and wide
regional diversification in both its impact and its epidemiology over the past thirty
years. These changes seem to be due to three factors:

- Firstly, a pronounced decrease in virulence of strains recovered both from wild
rabbits and farmed domestic rabbits. Since 1955, attenuated strains of myxoma virus
have been obtained from wild rabbits (14), and such strains have become more
numerous, accounting for over half of the strains examined by the end of the 1970's.
Since this date there seems to have been a slight increase in virulence (3).

- Appearance of wild rabbit populations genetically resistant to myxomatosis.
First observed in Australia (24, 25), such resistance was next seen in England (30).
Some experiments conducted on French rabbits indicate that the same process is also
present in France (Arthur, unpublished data). However, this phenomenon seems to
be extremely variable from place to place.

- The diversity of vector situations. The importance and role of the principal
myxomatosis vectors (fleas and mosquitoes) seem to differ widely between regions,
but the following facts have been established:

  a) An abundance of Culicidae in the Mediterranean region, and throughout
southern France, associated with an absence of fleas during summer. Thus in the
Camargue a rabbit may be bitten 300 to 1,200 times in 24 hours by over 12 species
of mosquitoes (22), while in the Rhone-Alps region there are 10 species which may
bite a rabbit 1-40 times in 24 h (28), compared with 1-4 bites in 24 h by 5 mosquito
species in the Paris region (33).

  b) Dominance of fleas in northern France associated with a virtual absence of
mosquitoes. Fleas are most prevalent between September-October and April-May,
with a peak flea burden of 200-300 per rabbit in February-March. This figure falls
to 60-120 fleas in the Paris region and 20-30 in southern France, with peak prevalence
occurring in the same months. In northern France and the Paris region, fleas are
present throughout the year, with a minimum of 10-20 fleas per rabbit in July-August
(20).

There have also been major changes in both wild and farmed rabbit populations.
Following the ravages of myxomatosis in wild rabbits between 1952 and 1970, and
also changes in farming practices and the environment, the distribution of wild rabbits
has undergone profound changes. In fact, the rabbit is no longer distributed
throughout France, but is found in "pockets" separated by empty zones varying in
size. Rabbits are present on no more than 40% of sites in two-thirds of the
Departments of France. They are distributed evenly throughout Brittany, which has
the highest densities (2), but occur in only 10% of sites in eastern Departments (1).
At the same time, the structure of rabbit farming has changed. Most rabbits are still
kept in small units of a few breeding does, the produce of which is consumed by
the owner (89% of all units) (23), but more rational production methods are beginning
to develop with the creation of intensive units housing several hundred does, and
accounting for about half of the 160-180,000 tonnes of rabbit meat produced per
year (32).
CLINICAL FEATURES OF THE DISEASE

Two clinical forms are recognised today, namely:

- The typical and classical **nodular or myxomatous form**, in which a primary myxoma forms at the site of inoculation of virus after an incubation period of 6-10 days (most often at the base of the ear flap or around the orbit). It rapidly develops into an inflammatory, tender swelling of the tissues of the head, with intense acute blepharoconjunctivitis (swollen eyelids and profuse lacrimation, becoming a purulent discharge). Within a matter of hours the rabbit is unable to open its eyes because of pus. After 2-3 days the inflammation spreads to the anogenital region, which appears swollen, taugh, hot and tender; it is at first pinkish, becoming red and then dark violet. The secondary myxomas of cutaneous generalisation may form anywhere on the body surface, but most often at the base of the ears and on the face, leading to the characteristic appearance of a leonine face and drooped ears. The nodules are of elastic consistency (sometimes reaching the size of a hazel nut) and are isolated or confluent, cold, insensitive to touch and incorporating skin, with an exudative aspect. Histologically these are pseudotumours or pseudomyxomas. Clinical signs which enable this form to be identified macroscopically are: a) prominent and numerous myxomas, particularly on the face; b) numerous ear lesions leading to drooping of ear flaps; c) respiratory disorders; d) swelling of eyelids with suppuration which may or may not be accompanied by conjunctivitis; e) pronounced oedema of genital organs. Death occurs in about ten days (after the onset of signs) from exhaustion, for the blind rabbit can no longer move nor feed. It is prone to secondary infections, or may die from inanition, or even asphyxia when lesions block the upper respiratory passages.

In addition to this acute course, invariably fatal, there are also subacute forms which lead to death after 20-30 days, or even mild forms which may be followed by recovery. A few small myxomas appear on the face (tip of the nose, eyelids, base of ear flap) with little or no exudation; they are flat and rapidly dry to form crusts. The crusts fall off after about 15 days to leave a scarred area which remains bald for several weeks. Genital complications (orchitis, oophoritis) accompanied by sterility and infertility (usually only temporary) are by no means rare, and they can partly prevent multiplication of the population.

- **Respiratory or non-myxomatous form.** This new form, which has appeared in France recently, has a longer incubation period (1-3 weeks), and is manifested by eye involvement (swelling) with genital and, above all, nasal lesions, accompanied by lacrimation and a mucopurulent nasal discharge. There may be some pink or red congestive spots on the ears, but no nodular skin lesions. There are degrees of severity comparable to those of the classical form. From the macroscopic aspect, this type of myxomatosis is characterised by: a) fewer and smaller myxomas; b) swelling of the eyelids is rapidly accompanied by severe, purulent conjunctivitis; c) coryza is always present, at first mild and serous, then severe and mucopurulent, with formation of crusts which obstruct the nostrils; d) occasional presence on the ears of simple, congestive macules or small ecchymotic suffusions. Initially described in intensive husbandry of domestic rabbits following inoculation of strain S.G. 33 vaccine (6), this clinical form has also been observed among rabbits kept under traditional husbandry and in wild rabbits. Of debatable origin (viral mutation or expression of an infection hitherto latent), this form of myxomatosis is accompanied by a change
in viral pathogenicity, and also by frequent occurrence of sterility and abandonment of newborn litters by farmed does.

**EPIDEMIOLOGY**

**FREQUENCY AND IMPORTANCE OF THE TWO FORMS OF MYXOMATOSIS AMONG WILD AND DOMESTIC RABBITS**

With the difference in management of the various enterprises, different types of disease may be observed. Most breeding is now conducted within closed buildings housing at least 20-30 breeding does. In such cases the microclimate is often unsuitable (excessive ventilation, high ammonia concentration, high animal density), and here myxomatosis generally assumes a respiratory form. There is no obvious seasonal fluctuation in the disease, and cases can occur throughout the year. The morbidity rate is slight (5-40%), the mortality rate lower (30-35%), and the incubation period as well as the evolution of the disease are longer (17-28 days). This viral infection is often associated with respiratory disease (coryza, pasteurellosis, pneumotropic viruses), which weakens the rabbits. On smaller rabbit farms the cages are often in the open air, sometimes protected by a roof. They are seldom provided with mosquito screens (less than 28% of traditional premises in the Rhone) (23). Moreover, the rabbits are usually kept in hutches of fibro-cement or wood, and not made entirely of wire as in the larger units. Under such conditions the average duration of myxomatosis is about 15 days with a maximum of 45 days. Cases occur mainly in summer and early autumn (as in the example of the outbreaks in the commune of Courtenay, Department of Isère; Fig. 6) (28). Coincidence in space and time with outbreaks of myxomatosis in wild rabbits has been noted (P. Duclos, personal communication). The morbidity rate is close to 50% and the mortality rate about 70%. Clinical signs are similar to those of typical sylvatic myxomatosis.

Both forms of myxomatosis in wild animals may be encountered at the same site. Although the "non-myxomatous" form occurs most often in populations of high density, with some degree of immunity, there is as yet no information on any geographical distribution of the different forms, or on the possible existence of a pluri-annual cycle with a succession of epizootics in which "non-myxomatous" virus dominates, separated by the sudden appearance of more lethal outbreaks in which "nodular" virus is dominant. Fig. 7 depicts the different forms of myxomatosis encountered, and their virulence during four years in part of the Paris region. Note that during a "non-myxomatous" outbreak (in 1980) the proportion of rabbits infected was low, and that the only strain of virus recovered between epizootics was of this type (July 1981). In other years the strains isolated were mostly of the classical type, even though cases of "non-myxomatous" disease also occurred. The presence of highly virulent strains was generally associated with a high proportion of infected animals (1982). However, in almost all epizootics (1979, 1981, 1982), different virulent strains of the same type were present simultaneously.

**EPIDEMIOLOGICAL CYCLE OF MYXOMATOSIS IN WILD RABBITS**

The cycle is shown in Fig. 8. The seasonal and annual variations seen in the field result from the interaction of three elements: an abundance of rabbits, immune status
Seasonal and annual incidence of myxomatosis
in the commune of Auffargis (Yvelines)
Presence and frequency
of different forms and strains of myxomatosis, 1979-1982

(Arthur, unpublished data)
Fig. 8
Epidemiological cycle of myxomatosis
during winter and in early spring, myxomatosis is spread mainly by the rabbit flea, *Spilopsyllus cuniculi*. Most cases of direct transmission also occur during this period. In this type of outbreak the speed of virus spread is usually slow.

Annual variations in morbidity and mortality are also dependent upon climatic features, since wet years favour the multiplication of mosquitoes and the spread of the disease, while diminishing the number of young rabbits through drowning in their burrows. Hot years favour rapid recovery from the disease (8) and limit vector development. On the contrary, there are numerous young rabbits, which are very susceptible to the virus.

There are three hypotheses concerning maintenance of the virus during the intervals between epizootics:

- *a*) Persistence of virus on mouth parts of the fleas, which can remain in a quiescent state for some time within uninhabited burrows (18);
- *b*) Conservation of virus in soil of the burrow, rabbits becoming infected during summer rearrangement of the warren (18);
- *c*) The virus may circulate during winter as asymptomatic infection in rabbits which have become immune during the summer epizootic (36).

**EPIDEMIOLOGICAL CYCLE OF MYXOMATOSIS ON RABBIT FARMS**

Information obtained through investigation of rabbit farms reveals the existence of two types of myxomatosis.

- Under **intensive husbandry** within closed buildings, regular disinfection does not seem to play a part in the appearance of the disease. Various strains of virus isolated from infected animals (almost exclusively of the "non-myxomatous" form) on this type of premises have shown a greater ability to disseminate than that of typical strains. In contrast to the typical virus, transmission regularly takes place by the airborne route with inhalation of infective particles. In the laboratory it is possible to reproduce transmission of these "respiratory" virus strains from cage to cage without a vector and without direct contact (6). There may be a state of occult latent infection, although this has not been proved so far. This type of infection probably exists only in certain premises, and has been observed solely under poor conditions (bad ventilation, high frequency of respiratory disease, etc.). In such cases, myxomatosis occurs in an irregular cycle, with episodes throughout the year, and it is transmitted exclusively by the airborne route.

- Under conditions of **traditional husbandry**, strains of virus isolated are usually of the "nodular" form. Most outbreaks occur in autumn, between October and December (23). The fact that premises rendered free from insects are rarely affected leads to a suspicion of transmission by winged insects. Variations in the impact of the disease in such premises can be explained by two reasons in particular, as follows: firstly, the rate of replacement of breeding animals through outside purchases and, secondly, due to the differences in the degree of care and supervision. Depending on the thoroughness of application of prophylactic measures, epizootics may be regular, rare or even non-existent.
POSSIBLE CONNECTIONS BETWEEN DOMESTIC RABBIT AND WILD RABBIT CYCLES

Among intensively managed rabbits, the probability of reinforcement of the disease cycle among domestic rabbits by virus from wild rabbits seems to be very low or nil. Most of the epizootics observed have arisen from recent introduction of animals from premises which have experienced infection during the previous 2-3 months (6). Such animals are either in an incubation period longer than normal, or they are asymptomatic carriers, the virus becoming active as a result of stress brought about by the transfer to new premises. The possibility of wild rabbits becoming infected from sick animals kept in this type of premises is practically nil, for sick animals are usually soon killed and destroyed.

Under traditional husbandry the nature of the disease and its coincidence in space and time with wildlife outbreaks of myxomatosis lead to the suspicion of infection from wild rabbits. A study by Puech (28) of the occurrence of members of Culicidae in barns, stables and open sheds in the Rhone-Alps region revealed the presence of three mosquito species between the end of October and the end of March. Furthermore, the course of myxomatosis observed by Puech showed a delay of 6-8 weeks between the epizootic peaks in wild and domestic rabbits, the domestic rabbit peak coinciding with the arrival of mosquitoes within farm buildings. The strict microclimatic requirements of mosquitoes govern their choice of hibernation sites, and explain the disparity in the distribution of affected hutches, for one hutch may remain free from infection while another just 500-1,000 m away becomes infected. Cases of myxomatosis among farmed rabbits in winter may be explained by a temporary lifting of hibernation, during which the mosquitoes take a blood meal; mosquitoes usually hibernate in haylofts close to the cages. Some mosquitoes have been found to be carrying the virus upon their emergence from hibernation, and these could be the origin of outbreaks on rabbit farms in spring. However, simulation testing of virus survival has shown that few mosquitoes are still alive 4-6 months after an infection followed by hibernation. Storage of the virus in the laboratory at low temperature for four months results in considerable attenuation, supporting field observations that mosquitoes emerging from hibernation yielded only attenuated strains of virus (28). One may therefore conclude that there is little possibility of a new outbreak among wild rabbits from an outbreak among domestic rabbits, for infection of domestic rabbits is rather the final stage of sylvatic myxomatosis. The summer outbreaks which occur on this type of premises are related to the close proximity of a large population of wild rabbits, as well as the multiplication of winged vectors in certain years. The low incidence of "non-myxomatous" forms in this type of premises is connected with the failure of vectors to carry strains of such low virulence (35, 8).

Wildlife myxomatosis has its own cycle, apparently unrelated to myxomatosis in domestic rabbits. The permanence of the virus in populations of wild rabbits remote from human settlements provides additional proof of the independence of the wildlife cycle.
DISEASE CONTROL

VACCINES AVAILABLE AGAINST MYXOMATOSIS

Both heterologous and homologous vaccines can be used for immunising rabbits against myxomatosis.

Heterologous vaccines

Heterologous vaccination makes use of the immunological relationship between the viruses of myxomatosis and rabbit fibroma. Protection commences around the fifth day, and may last for more than six months in some rabbits. In fact, the degree and duration of protection are extremely variable and depend on many factors, particularly the route of administration, age of rabbit and individual receptivity. Intradermal inoculation of young rabbits 4-6 weeks of age provides adequate protection, but it does not last long, and only 30% resist challenge infection after three months. The degree of protection is less satisfactory in adult rabbits, and in the best cases only 70% are protected after three weeks, about 50% after three months, and smaller proportions (at most 30-40%) after six months (9). However, the postvaccinal reaction to heterologous vaccines is exceptionally mild (15).

Homologous vaccines

Among the modified strains of virus, the one most widely used in France is strain S.G. 33 of Saurat-Gilbert, developed at the Toulouse National Veterinary School* (31). The immunogenicity of this strain is very good. Protection may be present as soon as three days after intradermal inoculation, and may persist for a year or more in some rabbits. In this case as well, route of injection and age of animal are the chief factors governing the immune response. The protective ability of homologous vaccine is clearly superior to that of heterologous vaccine. When young rabbits are vaccinated first at 2-3 months of age, there is no need for a booster dose before one year has elapsed, unless there is exceptional risk of infection. Even when this risk is present, it is recommended that the second dose of vaccine be given no sooner than three months after the first dose, as otherwise the animal may fail to respond. Conversely, vaccination at an earlier age, such as 3-4 weeks, may fail even when a vaccinal myxoma develops, and a second dose will be necessary after three months. The safety of the vaccine has been questioned, and various incidents have led the manufacturer to modify the vaccination procedure, namely: a heterologous vaccine for primary vaccination, followed by homologous vaccine a month later. Various trials have shown that strain S.G. 33 is effective and safe for rabbits in good health, but it may lead to respiratory disease or abortion in 1-2% of vaccinated rabbits in certain intensive units (4, 13).

* Other vaccine strains have been developed recently in Spain, Italy and Hungary in particular. The major differences between them lie in their immunogenic properties and in the nature of the postvaccinal lesions.
APPLICATION OF PROPHYLAXIS TO RABBIT FARMING

Since various recent trials have demonstrated the efficacy of strain S.G. 33, including its use in incipient outbreaks (16), as well as its innocuity (5), the protection of farmed rabbits should be based on this type of vaccine, with or without a heterologous vaccine.

Traditional husbandry

Under conditions when the rabbits are exposed to the bites of arthropods infected from a wild rabbit source, vaccination is essential. Annual vaccination of all adult rabbits with strain S.G. 33 is carried out during the period of seasonal anoestrus. Young rabbits should be vaccinated systematically upon reaching 4-5 weeks of age, with booster doses for all these animals kept for longer than three months. If the premises has been severely affected in the past, Shope's fibroma virus is best used for the primary vaccination.

Intensive husbandry

In principle, protection based on preventing access by arthropods should make it unnecessary to vaccinate against nodular myxomatosis. Even if insects do enter the building, insecticidal treatment coupled with the removal of infected rabbits should be sufficient to control the disease. The respiratory forms of the disease create different problems, because it is difficult to organise effective precautions in the absence of precise epidemiological data. If the health standard of the unit is high, homologous vaccination may be adequate. In reality, it is often more appropriate to choose fibroma virus vaccine, or a combination of both methods of vaccination. A major disadvantage of this double vaccination is that, in some rabbits, the residual immunity derived from heterologous vaccine may partly or completely inhibit the effects of vaccination with strain S.G. 33 vaccine if the latter is inoculated within one or two months. Such a procedure presupposes a check of whether the vaccination has taken, followed when necessary by a booster dose after 4-6 months.

PROPHYLACTIC MEASURES APPLICABLE TO WILD RABBITS

Vaccination is the procedure used most so far. It was based originally on the use of heterologous vaccine prepared from Shope's fibroma virus, but is performed almost exclusively with strain S.G. 33 vaccine. However, since it is difficult to capture wild rabbits, this vaccination is practically confined to individuals released during operations for repopulation for hunting purposes (between 400 and 500 thousand rabbits are released each year). The results seem to be very uncertain, and so far have not provided protection of a population from the virus.

The control of vectors, particularly fleas, based on the application of flea collars to rabbits, has given good results within enclosures (21), but cannot be applied satisfactorily in nature, because of the impossibility of catching enough rabbits. There have been various attempts to control fleas by insecticidal treatment of burrows, and some experiments to administer a systemic insecticide orally in a bait.

A different approach is currently being tried, using the rabbit flea as a vector of vaccine. Fleas carrying vaccine virus have been released during July and August,
the months during which half of the outbreaks occur, in order to inoculate rabbits with the virus when the fleas feed. While some vaccinations have succeeded under laboratory conditions, there are too many complications under field conditions to hope that this method can be of much use.

In fact, at present it seems rather difficult to introduce effective measures against the wildlife reservoir of myxomatosis, or even to limit the effects of the field virus.

CONCLUSION

While myxomatosis in domestic rabbits kept under traditional husbandry is directly related to, and is the final stage of the disease in wild animals, a new form of the disease with its own epidemiological features seems to have become established under intensive husbandry. Nevertheless, the economic consequences appear to be minor, and the disease can be controlled readily by an adequate vaccination programme. The intrusion of classical nodular myxomatosis into intensive premises can be stopped by means of disease barriers and regular insecticidal treatment. Under traditional husbandry the consequences vary according to the existence and abundance of wild rabbits in the vicinity and the type of building construction. Vaccination is seldom resorted to, even though it is the only remedy. As for the disease in wild rabbits, no preventive measures have proved entirely successful. The effects of the virus in wild populations will abate only through a change in the equilibrium between the disease and its host.

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REFERENCES

(see p. 955)