VARIATIONS IN THE EFFECTIVENESS OF COMMERCIAL INFECTIOUS FELINE ENTERITIS VACCINES IN PREVENTING VIRUS ENTERITIS OF MINK

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THE EARLIEST REPORT (8) ascribing the cause of an acute enteritis of mink to a virus appeared in 1949. Features of the disease and the extent of its distribution were described then and in other reports (1, 2, 5, 7, 10). In 1952, observations were recorded (9) which confirmed the viral etiology of the disease and which led to the conclusion that the virus causing enteritis in mink was the same as, or closely related to, the virus of infectious feline enteritis (feline distemper, feline panleucopenia). The mink virus when given to young felines produced in them the clinical picture, mortality, leucopenia and intestinal lesions characteristic of infectious feline enteritis. This response of cats to the mink virus was prevented by convalescent mink serum, and commercial infectious feline enteritis antiserum prevented virus enteritis in mink. Virus enteritis in mink was found to be accompanied by leucopenia. The histopathological changes of the intestines of mink infected with virus enteritis closely resembled those changes found in the intestines of cats suffering from infectious feline enteritis. Possibly the extreme difficulty of maintaining control felines free of intercurrent infectious feline enteritis delayed confirmation of these findings. The transmission of infectious feline enteritis virus to mink and confirmation of the antigenic similarity of the mink and feline enteritis viruses have since been reported (3, 4).

The report (9) relating virus enteritis of mink to infectious feline enteritis also recorded the effectiveness of an homologous formalin-inactivated tissue vaccine in preventing virus enteritis both when used experimentally and in the face of an outbreak in the field. From 1951 to 1958, vaccine prepared at the Ontario Veterinary College from mink which had died in natural outbreaks was used very successfully to reduce losses when other outbreaks occurred. This homologous vaccine produced† from mink artificially infected at pelting time is now available commercially. Exhaustive tests have been recorded (6) which show this vaccine to produce excellent and enduring immunity when given as a single dose of 1 c.c. to mink kits just after weaning.

Before commercial homologous vaccine became available for prophylactic use, the supply of vaccine was dependent upon mink which had died in natural outbreaks. In order to seek an independent source of protection and to examine further the relationship of virus enteritis in mink and cats, the authors tested commercial infectious feline enteritis vaccine for its ability to protect mink against the mink virus. The feline vaccine was shown to be an efficient agent for this purpose (11). The report on this work also succeeded in dispelling some of the scepticism which had met the original proposition of the relationship of the two diseases.

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Subsequent to the publication (11) in 1956 on the value of infectious feline enteritis vaccine, feline vaccine prepared by various manufacturers was widely used by ranchers in Canada and the United States. Many ranchers have used these products with apparent satisfaction; others in Ontario became unwilling to do so because of outbreaks of virus enteritis despite vaccination. It will be shown that the use of certain brands of vaccine, lacking in antigenicity for mink, has led, in Ontario at least, to unwarranted prejudice by some ranchers against all vaccine of feline origin.

In the work just referred to (11) the dosage schedule used for mink was the same as that recommended for cats, i.e., two doses of 2 c.c. each, given subcutaneously, with one week intervening between doses. The product of only one manufacturer was tested on an adequate number of animals, and these mink had reached early maturity at the time of vaccination. Virus enteritis of mink is most devastating in young animals so that it is important to achieve effective protection as early as possible. The present experiment was designed to find out whether newly-weaned mink kits would respond to the vaccine and how quickly, if at all, they would develop satisfactory resistance to challenge. A brand of commercial infectious feline enteritis vaccine different from those previously tested was selected and the most economical use of labour and antigen was also studied.

Materials and Methods

Experimental animals. Five ranches on which virus enteritis had never appeared or had been absent for at least a year supplied mink kits ranging from 6½ to 8 weeks of age. Most of their dams had been vaccinated with infectious feline enteritis vaccine about ten months before the birth of the kits. Most of the kits were used to test vaccine dose levels of one or the other of two kinds of vaccine, and for these tests kits from different ranches and litters were distributed as randomly as possible among 36 test and control groups so that each ranch was represented in each group.

Vaccines. The vaccine ordinarily used in the prevention of infectious feline enteritis consists of a suspension in saline of tissues taken from cats at the height of infection. The virus is inactivated with formalin. Two doses of 2 c.c. each are given subcutaneously to cats one week apart. Another type of vaccine is composed of virus-bearing tissues suspended in an oily adjuvant. This is usually given intramuscularly to felines as a single dose of 1 c.c. In 1956 a feline vaccine of the adjuvant type was advertised for sale in Ontario for use in the prevention of virus enteritis in mink. The directions specified a single dose of 1 c.c. to be given subcutaneously.

In the main body of the work reported below, both types of vaccine were tested at various dose levels and mink were challenged at various periods after vaccination. The ordinary type vaccine and the adjuvant type vaccine will be referred to as "saline" vaccine and "adjuvant" vaccine respectively. Both types of vaccine were obtained from the same producer (Manufacturer A) but were prepared from different batches of infected feline tissues. In addition, and to be reported later in this paper as a separate item, saline vaccine from another source, Manufacturer B, was tested for potency in comparison with the saline product

TABLE I

PREVENTION OF VIRUS ENTERITIS OF MINK WITH INFECTIOUS FELINE ENTERITIS VACCINE: THE VALUE OF SALINE-SUSPENDED VACCINE (BRAND A) COMPARED WITH THE FAILURE OF AN ADJUVANT VACCINE PRODUCED BY THE SAME MANUFACTURER

Interval between first vaccination and challenge	Type of vaccine	No. of doses	Dose in c.c.	Route	No. challenged	No. sick	No. died
2 weeks	saline	2	2	Subcutaneous	6	1	0
	,,	2	1	,,	6	0	0
	,,	1	2	,,	6	1	1
3 weeks	saline	2	2	,,	6	0	0
	,,	2	1	,,	6	0	0
	,,	1	2	,,	6	0	0
4 weeks	saline	2	2	,,	6	0	0
	,,	2	1	,,	6	1	0
	,,	1	2	,,	6	1	1
6 weeks	saline	2	2	,,	4	0	0
	,,	2	1	,,	4	0	0
	,,	1	2	,,	5	1	0
				Totals	67	5	2
2 weeks	Saline & Adjuvant	1	1	Subcutaneous ,,	6	1	0
		1	0.5				
3 weeks	Saline & Adjuvant	1	1	,, ,,	6	0	0
		1	0.5				
4 weeks	Saline & Adjuvant	1	1	,, ,,	6	0	0
		1	0.5				
6 weeks	Saline & Adjuvant	1	1	,, ,,	5	0	0
		1	0.5				
				Totals	23	1	0
2 weeks	Adjuvant	1	1	Subcutaneous	6	6	5
	,,	1	1	Intraperitoneal	6	6	4
	,,	1	0.5	Subcutaneous	6	5	3
	,,	1	0.5	Intraperitoneal	6	6	4
3 weeks	Adjuvant	1	1	Subcutaneous	6	3	2
	,,	1	1	Intraperitoneal	6	3	1
	,,	1	0.5	Subcutaneous	6	4	3
	,,	1	0.5	Intraperitoneal	6	3	2
4 weeks	Adjuvant	1	1	Subcutaneous	6	5	4
	,,	1	1	Intraperitoneal	6	6	2
	,,	1	0.5	Subcutaneous	6	6	5
	,,	1	0.5	Intraperitoneal	6	5	3
6 weeks	Adjuvant	1	1	Subcutaneous	6	2	1
	,,	1	1	Intraperitoneal	4	3	3
	,,	1	0.5	Subcutaneous	6	5	4
	,,	1	0.5	Intraperitoneal	5	5	2
				Totals	93	73	48
2 weeks	Control	—	—	—	6	6	3
3 weeks	,,	—	—	—	6	5	2
4 weeks	,,	—	—	—	6	5	3
6 weeks	,,	—	—	—	4	3	3
				Totals	22	19	11

of Manufacturer A. Manufacturer B's product was drawn to our attention because of its apparent failure to establish adequate protection when used by ranchers.

The vaccines used were manufactured in the United States and were labelled "Feline Distemper Vaccine".

Vaccination. Saline and adjuvant vaccines procured from Manufacturer A were

given to groups of mink (Table I) in each of the following variations of dosage.

Saline Vaccine

A. Two doses of 2 c.c. each, given subcutaneously, one week apart.

B. Two doses of 1 c.c. each given subcutaneously, one week apart.

C. One dose of 2 c.c. given subcutaneously.

Adjuvant Vaccine

A. One dose of 1 c.c. given subcutaneously.

B. One dose of 0.5 c.c. given subcutaneously.

C. One dose of 1 c.c. given intraperitoneally.

D. One dose of 0.5 c.c. given intraperitoneally.

Saline and Adjuvant Vaccines

One dose of 1 c.c. saline vaccine and, simultaneously, at another site, one dose of 0.5 c.c. adjuvant vaccine, both given subcutaneously.

All mink were vaccinated for the first time on the same day and groups were withdrawn for challenge at appropriate intervals.

Challenge. Artificially challenged mink were given 5 c.c. of a 20 per cent saline suspension of infected liver and spleen by stomach tube. To ensure high potency the first challenge material was from the third rapid serial passage of the virus. A new passage was made for each challenge thereafter.

Groups of mink on each type of vaccine and dose variation were challenged at intervals of 2, 3, 4 and 6 weeks after their first dose of vaccine. It was originally planned to challenge all groups artificially, but, because of the consistency of results up to and including those tested at their fourth week, the remaining groups were subjected to natural exposure by placing them on a heavily infected ranch six weeks after vaccination.

All mink recorded as sick (Table I) were severely ill with unmistakable evidence of virus enteritis according to a previously established criterion (6).

Results of Challenge

An examination of the results of challenge (Table I) will show that there was no significant difference in the protection, or lack of it, induced by the different dosage levels of either type of vaccine, nor is there any apparent difference in response dependent upon the time of challenge after vaccination. A single dose of 2 c.c. of the saline vaccine appears to be as useful, within the limits of the challenge periods, as two doses of 2 c.c. given one week apart. On the other hand, there appeared to be no protective response to the adjuvant vaccine at the dose recommended by the manufacturer. Therefore the results for all challenge periods of all dose levels for the particular type of vaccine have been combined (Table I) and may be summarized as follows:

Of a total of 22 unvaccinated controls, 19 became ill, and of these 11 died. Of a total of 93 mink given adjuvant vaccine, 73 became ill, and of these 48 died. Of a total of 67 mink given saline vaccine, 5 became ill, and of these, 2 died.

Simultaneous doses of 1 c.c. of saline vaccine and 0.5 c.c. adjuvant vaccine gave good protection. Of a total of 18 mink so vaccinated, one became ill and it recovered. In view of the complete failure of the adjuvant vaccine alone to give protection, the protection is believed to result from the 1 c.c. dose of saline vaccine.

Comparison of Two Saline-Suspended Vaccines from Different Manufacturers

During the course of experiments with products of Manufacturer A as recorded above, our attention was drawn to a saline vaccine of feline origin produced by Manufacturer B which, in the field was apparently failing to produce adequate protection. About 30,000 mink had been vaccinated with this brand, usually with a single dose of 2 c.c. The ranchers had purchased it at a price per dose well below the price asked by other manufacturers for the same type of product. The vaccine was considerably less turbid than we had learned to expect in satisfactory products. A hitherto unopened vial, which had been held under refrigeration since purchase, was tested before its date of expiry.

Mink were obtained from a ranch on which virus enteritis had never appeared and were divided at random into three groups. One group received two doses of 2 c.c. each of Brand A vaccine subcutaneously, with one week intervening between doses and another group was dosed in the same way with Brand B vaccine. The third group served as controls. Two weeks after the first vaccination the three groups were challenged.

Results

The results are recorded (Table II). It will be seen that complete protection was afforded by Brand A saline vaccine against a potent challenge, whereas Brand B vaccine afforded no protection. Brand A produced complete resistance in 5 mink to a challenge which caused 5 of 6 controls to become sick. Three of these control mink died. On the other hand, of 5 mink which had received Brand B vaccine, 5 became sick and 3 died.

TABLE II

Failure of a Saline-Suspended Infectious Feline Enteritis Vaccine (Brand B) to Protect Mink Against Virus Enteritis

Interval between first vaccination and challenge	Vaccine	No. of doses	Dose in c.c.	Route	No. challenged	No. sick	No. died
2 weeks	Brand A	2	2	Subcutaneous	5	0	0
	Brand B	2	2	,,	5	5	3
	Control	—	—	—	6	5	3

Summary and Conclusions

The previously reported usefulness of saline-suspended formalinized infectious feline enteritis vaccine in the prevention of virus enteritis of mink is confirmed. In addition, we have found in tests of one product of this type, that a single dose of 2 c.c. and probably as little as a single dose of 1 c.c., will induce satisfactory immunity in newly-weaned mink kits. Substantial resistance to artificial challenge was evident as early as two weeks, and also at three and four weeks after a single dose of vaccine. Kits similarly vaccinated were also resistant to severe natural exposure to the disease six weeks after vaccination.

On the other hand, an infectious feline enteritis vaccine, prepared by the same manufacturer, containing an oily adjuvant and advertised by him as a preventive

for mink enteritis, failed to induce protection When given to mink subcutaneously as the advertiser directed, or when given intraperitoneally, challenge at 2, 3, 4, and 6 weeks after vaccination showed the animals still to be susceptible. It should be noted that vaccines containing oily adjuvants are usually given intramuscularly. This route, however, is impracticable in young mink.

Nor are all commercial infectious feline enteritis vaccines of the saline type satisfactory for the prevention of virus enteritis of mink. A saline-suspended tissue vaccine produced by another manufacturer, sold in large quantities to ranchers at an unusually low price, was used in the field with disappointing results. When tested experimentally using two doses of 2 c.c. each, given seven days apart, this vaccine failed to establish protection in mink. As judged by turbidity, in comparison with satisfactory products, the tissue content of this vaccine may have been low.

Résumé et Conclusion

On confirme les rapports antérieurs sur l'efficacité du vaccin formolé en suspension saline comme moyen de prévention de l'entérite infectieuse du vison. De plus, en expérimentant avec un tel produit, on trouva qu'une dose de 2 ml. et même qu'aussi peu qu'une seule dose de 1 ml. peut produire une immunité suffisante chez les jeunes visons récemment sevrés. Lors de cette expérience, on constata une résistance marquée à l'infection artificielle seulement deux semaines après l'injection d'une seule dose de ce vaccin; cette résistance fut aussi remarquée après trois et quatre semaines. De jeunes visons vaccinés de la même manière furent résistants à l'infection naturelle six semaines après leur vaccination.

D'un autre côté, un vaccin en suspension huileuse, préparé contre l'entérite infectieuse du chat par le même laboratoire et recommandé comme devant être efficace pour prévenir l'entérite infectieuse du vison, n'eut aucun effet protecteur. Ce vaccin administré par voie sous-cutanée ou intra-péritonéale n'eut pas d'effet immunisant lorsqu'on infecta artificiellement les visons à 2, 3, 4 et 6 semaines après leur vaccination. Habituellement les vaccins en suspension huileuse s'administrent par voie intra-musculaire; cependant on ne peut utiliser cette méthode chez le jeune vison.

Toutefois les vaccins commerciaux en suspension saline contre l'entérite infectieuse du chat ne sont pas tous efficaces. Un vaccin semblable préparé par un autre laboratoire et vendu en grande quantité à prix réduit aux éleveurs fut employé avec des résultats peu satisfaisants. On expérimenta ce vaccin en donnant 2 doses de 2 ml. chacune à 7 jours d'intervale sans produire d'immunité chez le vison. A en juger par sa turbidité en le comparant à des produits semblables, ce vaccin contenait peu de tissu en suspension.

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