Acta vet. scand. 1983, *24*, 499—511.

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AN OUTBREAK OF EXCESSIVE NEONATAL MORTALITY IN FOUR DANISH MINK FARMS

II. ANALYTIC EPIDEMIOLOGICAL INVESTIGATIONS

By

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BØTNER, ANETTE G. and POUL H. JØRGENSEN: *An outbreak of excessive neonatal mortality in four Danish mink farms. II. Analytic epidemiological investigations.* Acta vet. scand. 1983, *24*, 499—511. — Data collected from an outbreak of excessive mortality of mink kits in 4 Danish mink farms in 1982 were analysed. The mortality of the mink kits was found to be highest for the kits from Aleutian Disease (AD)-positive females, and the Scanblack mink was found to be the most frequently affected mink type. Furthermore the mortality was found to depend on the farm of origin and to be highest for the lastest born kits. The age of the females and their location in sheds were found not to influence the mortality of the kits. However, the mortality for the Pastel mink decreased with increasing distance from the Scanblack mink. The possibility that the excess mortality of the kits might be due to an AD-virus infection is discussed.

mink; neonatal mortality; mink kits; Aleutian Disease; analytic epidemiology.

A suddenly increased mortality among mink kits was recorded in May 1982 in 4 Danish mink farms, here designated farms A, B, C, and D. All the affected kits exhibited pronounced symptoms of respiratory disease with accelerating dyspnoe, and death followed within 24 h after the manifestation of the symptoms. The etiology of the disease is so far uncertain. A detailed description of the events has been given by *Jørgensen & Bøtner* (1983). The present report contains an analytic epidemiologic study concerning possible causal associations between the mortality of mink kits and different factors.

MATERIALS AND METHODS

A description of the populations of the 4 farms and of the mortality throughout the investigation period has been given in the preceding publication by *Jørgensen & Bøtner* (1983), where the prevalence of Aleutian Disease (AD) in the 4 farms was also discussed.

Kid mortality was calculated for 2 time periods: *early neonatal mortality rate (ENMR),* i.e. the proportion of kits dying between birth and May 15th out of the number of liveborn kits; and as *late neonatal mortality rate (LNMR),* the proportion of kits dying throughout the remaining part of the investigation period (May 15th to June 30th) out of the number of kits alive on May 15th. The associations between the mortality of mink kits and different factors were investigated mainly concerning the LNMR. The procedure for indirect standardization was applied according to *Foldspang et al.* (1981). When standardization was made for differences among mink types, the overall LNMR for each mink type was applied to the respective population, and when the standardization was made for differences in AD-status the overall LNMR for AD-positive and AD-negative, respectively, was applied to the particular population. The standard mortality ratio (SMR) is the ratio between the observed and the expected (standardized) number of deaths. The standardized LNMR is the product of the SMR of the examined population and the overall LNMR. It must be noted that the overall LNMR's for farm A and for farm C in Table 1 and Table 2 do not agree. This is due to differencies in the size of the populations because of lack of information about the AD-status for some of the females.

Statistical comparisons between unadjusted rates were made by means of the common chi-square test. Evaluation of the effect of indirect standardization was made by means of chi-square test where the expected numbers originated from the standardization procedure (*Foldspang et al.* 1981).

RESULTS

Relationship between AD status of the dam and mortality of kits

The relation between the AD-status of the females and the late neonatal mortality of the kits was investigated for farm A and C. Only for these farms was the individual AD-status known for most of the females.

Table 1. LNMR (%) in farms A and C, related to the AD-status of the females. Only females with known AD-status were included.

AD-status of the females	LNMR (%) among kits	
	farm A	farm C
Positive	19.5	9.1
Negative	4.8	1.0
Total	8.9	5.7

The late neonatal mortality rates were significantly ($P<0.001$) higher among kits from AD-positive mothers than from AD-negative mothers within the farms (Table 1). At farm A there was a relative risk (ratio of LNMR's for AD-positive/negative) of 4.1 and at farm C the relative risk was 9.1. By indirect standardization of LNMR for differences among mink types the relative risk for farm A changed to 2.3. This change is statistically significant ($P<0.001$). It is therefore concluded that mink type is a confounder for the association between AD-status and mor-

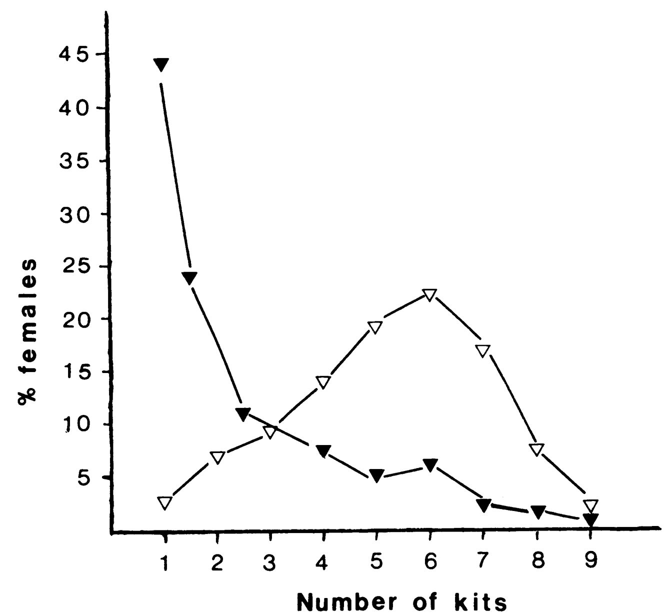


Figure 1. Farm A. Proportional distributions of number of kits per female at the beginning of the investigation period (▽—▽), and number of kits lost in the investigation period among females with late neonatal mortality (▼—▼).

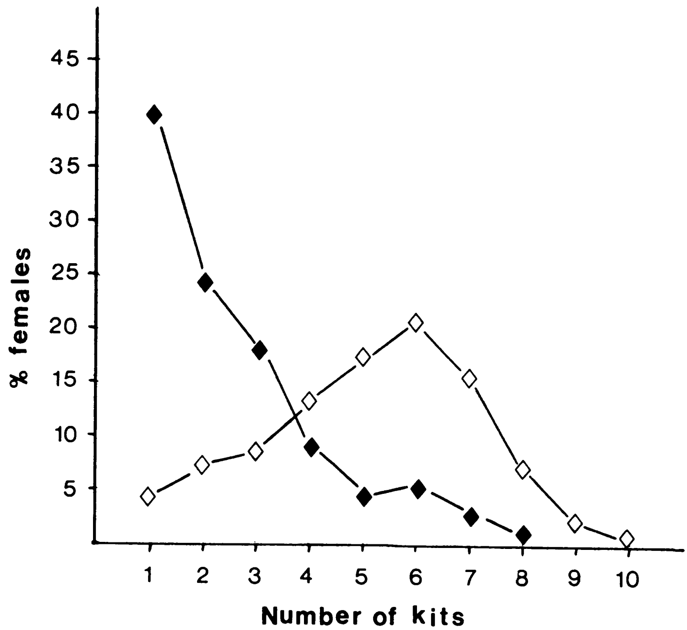


Figure 2. Farm B. Proportional distributions of number of kits per female at the beginning of the investigation period (◇—◇), and number of kits lost in the investigation period among females with late neonatal mortality (◆—◆).

tality of kits at farm A. However, the relative risk of 2.3 remains to reflect a significant difference in LNMR between kits from AD-positive and AD-negative females. The data from farm C did not support the same conclusion, as no significant difference was found between observed and expected number of deaths. Fig. 1 and Fig. 2 show, that most of the females with dead kits have lost only 1 kit and that the number of kits per litter at the beginning of the investigation period seems to be distributed around an average of 5 to 6. This implies that only a few females have lost the whole litter in the investigation period. Fig. 3 shows the percentage of AD-positive females at farm A related to the number of kits lost in the investigation period. There does not seem to be an association between the percentage of AD-positive females and the number of dead kits per female. On the other hand there is a significant difference in the percentage of AD-positives at this farm between females with and without kits lost in the investigation period: % AD-positive among females with

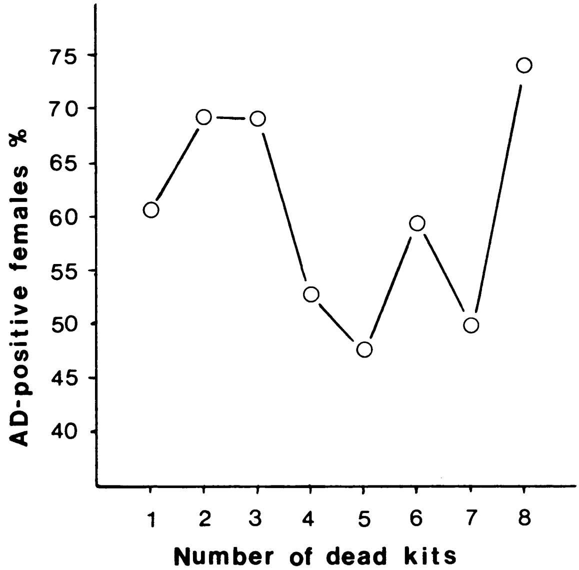


Figure 3. Farm A. Proportion of AD-positive females by number of kits dying in the investigation period.

affected kits was 62.3, while % AD-positive among females without affected kits was 18.4.

Relationship between mink type and mortality of kits

By comparing the mink types a statistically significant difference ($P<0.001$) in mortality of kits between the types is noticed (Tables 2, 3 and 4). Scanblack had the highest ENMR and LNMR. Mogul and to some degree Pearl are not well repre-

Table 2. LNMR (%) at the 4 affected farms. For farm D the rates have been calculated for the period from birth to the end of the investigation period. For farm C the period ends June 8th. The number of dead kits at farm A has been corrected.

	LNMR (%)			
Type	farm A	farm B	farm C	farm D
Scanblack	14.6	30.4	11.4	40.5
Pastel	4.7	14.1	2.3	14.3
Pearl	14.4	—	0.9	—
Mogul	1.8	—	—	—
Total	9.9	22.0	6.1	25.5

Table 3. Relative risk between Scanblack and Pastel at the 4 affected farms. Number of dead kits at farm A has been corrected (as explained in the preceding paper).

	Farm A	Farm B	Farm C	Farm D
RR (Scbl/Past)	3.1	2.2	5.0	2.8

Table 4. Early neonatal mortality rate, ENMR (%), in farm A and B.

	ENMR (%)	
Type	farm A	farm B
Scanblack	7.2	17.8
Pastel	1.5	8.6
Total	4.5	13.3

sented as far as their numbers. The differences in ENMR's and LNMR's and relative risks among farms are not immediately intelligible. It seemed reasonable to investigate if the AD-status of the females had a confouding influence on the relation between the types and the LNMR of the kits. This was done by means of the indirect standardization method for LNMR at farm A and C, where the results of the AD-tests were known for the individual females.

The differences in LNMR of kits between the types remains after the standardization. Compared to the reference population Scanblack had a mortality of 115.4 % while the mortality for Pastel and Pearl was 71.6 % and 67.4 %, respectively (Table 5). The difference between observed and expected number of deaths is statistically significant ($P<0.001$) for both Scanblack and

Table 5. LNMR (%) before and after indirect stadardization for differences in AD-status at farm A. The numbers are not corrected. SMR = standard mortality ratio. The overall LNMR of the farm was used as reference.

Type	LNMR (%) before standardization	SMR	LNMR (%) after standardization
Scanblack	14.1	1.154	10.3
Pastel	3.9	0.716	6.4
Pearl	6.8	0.674	6.0
Total	8.9	1.000	—

Pastel, while corresponding significance is not found for Pearl ($P>0.01$). This might be due to a lower representation of this type in the population. According to these results, the AD-status of the females acted as a confounding factor in the relation between mink type and LNMR at farm A. Similar procedure was applied to the data for farm C. The LNMR for the types remained to differ appreciably, however, and the chi-square test did not show statistically significant differences between observed and expected number of deaths ($P>0.01$). For this farm therefore the AD-status did not act as confounder on the examined relation. The influence of type on the relation between AD-status and mortality of kits in the investigation period at farm A and C has been described above.

Relationship between mortality of kits and their location in sheds

The influence of location at birth, i.e. in which shed the kits were born, was investigated for farms A and B (Table 6).

The difference in LNMR between the sheds is found statistically significant ($P<0.001$) for both farms. However, the LNMR was highest in the sheds with Scanblack mink. Therefore the difference is thought essentially to represent differences between the types. Yet the tendency is that LNMR for the Pastel mink

Table 6. LNMR (%) at farm A and B in relation to location of the kits at birth. Number of dead kits at farm A has been corrected. Each shed contains 2 rows of covered cages.

Farm A			Farm B		
shed	type	LNMR (%)	shed	type	LNMR (%)
1	Pastel	4.5	3	Scanblack	15.2
2	Pastel	2.7	5	Scanblack	36.5
4	Pastel	4.6	6	Scanblack	35.8
5	Pastel	8.3	7	Scanblack	23.2
6	Scanblack	17.7	8	Scanblack	24.7
7	Scanblack	12.0	9	Scanblack	44.6
8	Scanblack	14.1	10	Scanblack	33.6
9	Scanblack	15.5	11	Scanblack	33.9
10	Pearl	14.4	12	Pastel	22.3
12	Scanblack/Mogul	4.9	13	Pastel	14.7
			14	Pastel	15.5
			16	Pastel	12.6
			15	Pastel	11.5
			20	Pastel	9.0

decrease with increasing distance from the Scanblack mink. This pattern is observed in both farms and might be due to transmission of the disease from Scanblack to Pastel. This implies horisontal spread of the disease in both farms. The relatively high LNMR for Pastel in shed 1 at farm A might be due to a climatically disfavourable location of this shed. A similarly high LNMR was found in shed 41 (Table 7). This shed has a similar location as shed 1.

LNMR in shed 3 at farm B was relatively low compared with LNMR for the other Scanblack sheds. This difference might be due to the different origin of the females, as the females in shed 3 originated from farm E, as discussed later. "Former sheds" means the location of the females in farm A before the transfer. The relationship of these sheds to the mortality of kits appears from Table 7. Also in this case there is a statistically significant

Table 7. LNMR (%) at farm B and farm C in relation to "former shed", i.e. location on farm A before the transfer.

Farm B			Farm C		
former shed	type	LNMR (%)	former shed	type	LNMR (%)
41	Pastel	20.3	46	Scanblack	10.2
43	Pastel	10.5	7	Scanblack	25.0
44	Pastel	10.4	6	Scanblack	20.8
45	Scanblack	35.4	46	Pastel	2.1
46	Scanblack	34.3	1	Pastel	2.5
49	Scanblack	29.8	10	Pearl	0.0
			50	Pearl	1.1

difference in LNMR ($P<0.001$) between the sheds. As earlier described there is a relatively high LNMR among progeny of females from shed 41 at farm A, which might be due to the extreme location of this hall. Any standardization procedure eliminating the influence of the types on the differences between sheds was not attempted; with respect to mink types the sheds are totally distinct and therefore the influence of the types on the difference in LNMR between the sheds is obvious.

Relationship between farm of origin and mortality of kits in farm B

Farm B introduced animals from both farm A and from a non-affected farm, farm E, before the beginning of the breeding season. On the basis of the collected data, it was possible to compare mortality rates for Scanblack introduced from the 2 farms and for Pastel introduced from farm A (Table 8). Unfortunately it was not possible to compare with animals which originated from the old stock of the farm, because of insufficient registration.

Table 8. LNMR (%) at farm B in relation to farm of origin.

Farm of origin	Type	LNMR (%)
Farm E	Scanblack	15.1
Farm A	Scanblack	33.3
Farm A	Pastel	14.1

All 3 groups show excessive mortality of kits (Table 8), compared to non-affected farms as formerly described (*Jørgensen & Bøtner* 1983). The relative risk between Scanblack from farm A and Scanblack from farm E is 2.2 which is statistically significant ($P<0.001$). Furthermore a difference in risk between the 2 types from farm A is noticed. Also here the chi-square test shows statistical significance ($P<0.001$). This supports the association between type and mortality of kits mentioned above.

The date of birth in relation to mortality of kits

For farm A and B the LNMR's were calculated for each date of birth respectively, (Fig. 4). The LNMR increases the later the

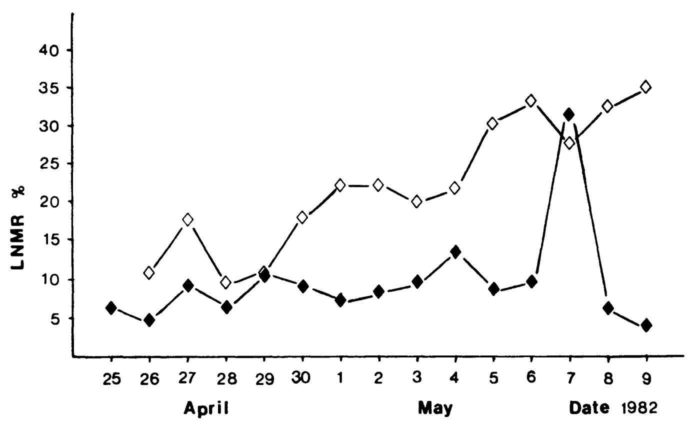


Figure 4. Late neonatal mortality rate related to date of birth. Farm A (◆—◆). Farm B (◇—◇).

kits are born. This is most pronounced at farm B. By dividing the season into 3 periods statistically significant differences in LNMR ($P<0.001$) were found between the periods on both farms (Table 9).

Table 9. LNMR in relation to birth period.

Birth period	LNMR (%) Farm A	LNMR (%) Farm B
April 25th—29th	9.9	14.9
April 30th—May 4th	8.6	20.5
May 5th—9th	12.9	54.1

Different dates of birth between the types do not cause the difference in LNMR between the periods mentioned as can be seen by comparing curves representing each type in Fig. 5 and Fig. 6. Furthermore, at farm B it is found that the increasing LNMR related to the date of birth are similar for Scanblack and Pastel (Fig. 7).

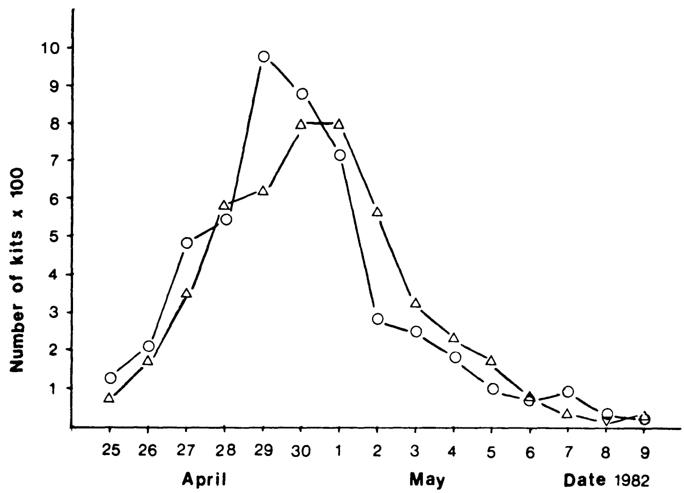
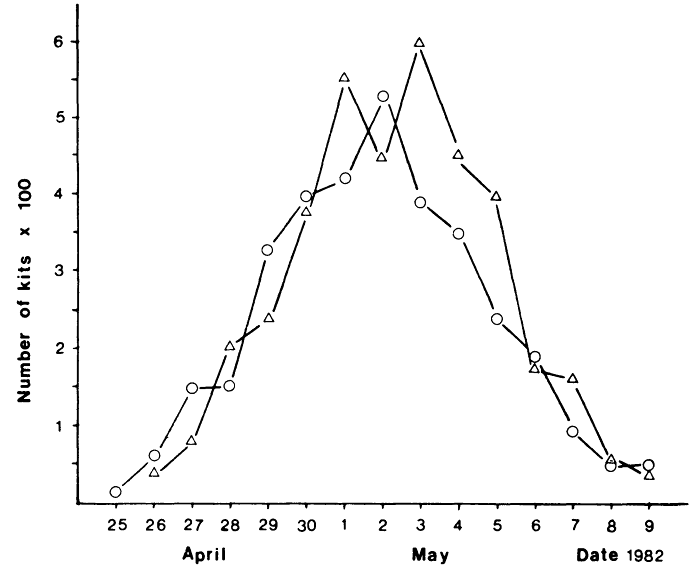


Figure 5. Farm A. Number of live kits born on the different dates. Scanblack (○—○); Pastel (△—△).

The age of the females in relation to mortality of kits

At farm B, C and D nearly all the females in the investigated sheds were of the same age (born in 1981). Therefore only data from farm A are used for the examination of the influence of the



F i g u r e 6. Farm B. Number of live kits born on the different dates. Scanblack (○—○); Pastel (△—△).

age of the females on the mortality of kits. Table 10 shows that the mortality of kits (LNMR) does not depend on the age of the female. There is no statistically significant difference (P>0.01) in LNMR for the kits of females of different ages.

T a b l e 1 0. Farm A. LNMR (%) related to age of the females.

Females year of birth	LNMR (%)
1978	9.8
1979	7.3
1980	8.7
1981	9.5

DISCUSSION

The LNMR is found to be highest for the kits from AD-positive females, and since AD-virus have been detected in the lungs of the diseased kits (*P. Have*, personal communication) the excess mortality of the kits might be due to an AD-virus infection. Typical symptoms of AD differ very much from what was found in this outbreak, but *Bazeley* (1976) has described similar pathology in kits infected with AD in the first 2 months of life, with most acute lesions in the first month. A significant increase in LNMR is found for both Scanblack and Pastel the later the kits

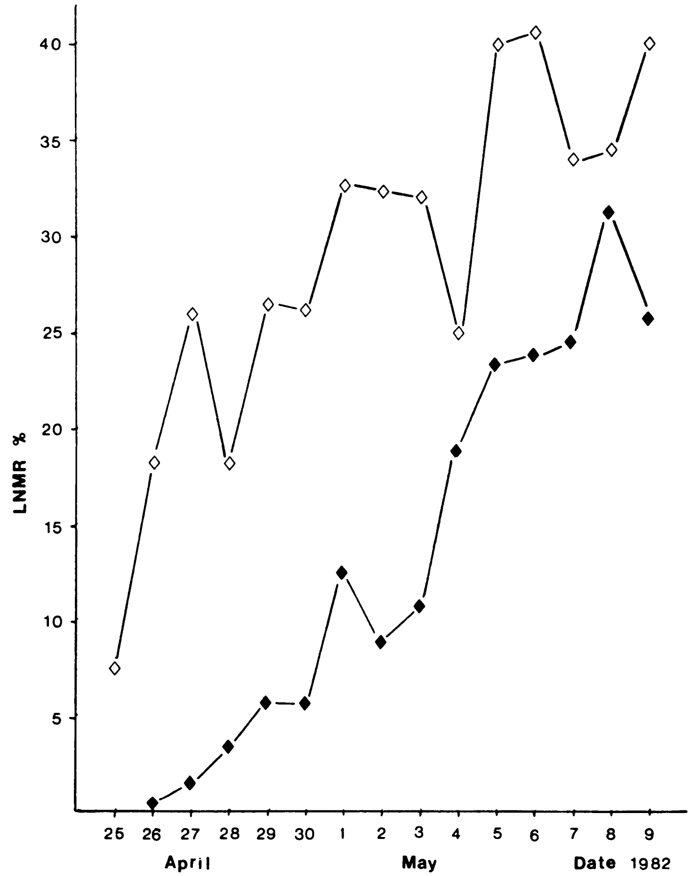


Figure 7. Farm B. Late neonatal mortality rate related to date of birth. Scanblack (◇–◇). Pastel (◆—◆).

are born at both farm A and farm B. Probably this is due to an increasing risk of exposure throughout the birth period with the growing population.

Differences existed in LNMR between the sheds in which the kits were born, but they mainly represented the difference between the types. However, the LNMR for the Pastel mink decreased with increasing distance from the Scanblack mink, which might indicate a spread of the disease in both farms from Scanblack to Pastel, possibly because of a lower susceptibility for the Pastel mink. Still, the Scanblack in shed 3 at farm B have a similar low LNMR as Pastel, which most probably is due to the fact that these females originated from farm E.

A difference in LNMR between the types is found to be significant even after standardization for AD-status, which at farm A was found to have a confounding influence. If the etiology of the disease is an AD-virus infection the cause of the type differences remains obscure. Yet, a spread of the disease among the Scanblack at farm A before the transfer in the spring 1982 and a subsequent infection of the Pastel and of the Scanblack originating from farm B might explain the lower LNMR for these groups. However, there was no barrier between the Pastel and the Scanblack at farm A, which makes a spread of the disease predominantly among the Scanblack immediately intelligible.

ACKNOWLEDGEMENTS

We thank Dr. P. Willeberg for his valuable advice and criticism. The investigation was supported by the Danish Fur Breeders Association.

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SAMMENDRAG

Et udbrud af excessiv neonatal hvalpedødelighed i 4 danske minkfarme. II. Analytisk epidemiologiske undersøgelser.

Data indsamlet fra et udbrud af excessiv hvalpedødelighed i 4 danske minkfarme blev analyseret. Hvalpedødeligheden fandtes størst iblandt hvalpene fra Aleutian Disease (AD)-positive mødre, og Scanblack minkene var den hårdest angrebne mink type. Derudover var hvalpedødeligheden afhængig af oprindelsesfarm og størst for de senest fødte hvalpe. Mødrenes alder og deres placering i haller influerede ikke på hvalpedødeligheden, dog såldes at hvalpedødeligheden for Pastel mink falder med stigende afstand fra Scanblack minkene. Muligheden for at den excessive hvalpedødelighed kan være forårsaget af en AD-virus infektion diskuteres.

(Received December 5, 1983).

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