Predicting recurrent PDV epizootics in European harbour seals *(Phoca vitulina)*

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ABSTRACT

Phocine Distemper Virus (PDV) caused mass mortality in European harbour seals *(Phoca vitulina)* in 1988 and in 2002. Both epizootics likely originated from *refugia* in Arctic seals, where data indicate PDV hops among populations and species. The metapopulation structure of host populations is suggested to be the reason why PDV is preserved among Arctic seals, since the high rate of spread of PDV would require much larger panmictic populations to maintain an infection. The pattern of sudden outbreaks of PDV is also seen in grey seals *(Halichoerus grypus)*, the only to date identified species that could act as a vector between Arctic and North Sea seal populations. Harbour seal populations along mainland Europe were below critical herd immunity levels by 3-5 years after the events, and thus vulnerable for new outbreaks, but historical data and the 14 years between the 2 epizootics suggest that harbour seals in the North Sea area are only rarely exposed to the infective agent. The risk for new outbreaks of the seal plague in North Sea harbour seals is likely linked to the dynamics of the disease in Arctic seal species as well as vector species.

Härkönen, T. and Harding, K.C. 2010. Predicting recurrent PDV epizootics in European harbour seals *(Phoca vitulina)*. *NAMMCO Sci. Publ*. 8:275-284.

INTRODUCTION

A majority of epizootic diseases affecting domestic and wildlife populations originate from reservoir species where they are endemic, thus infections are maintained without the need for external inputs. Illustrative examples are blue tongue disease which is caused by an orbivirus probably originating from African ungulates (Bekker 1934), rabies present in many species of carnivores (Childs 2002), and severe acute respiratory syndrome (SARS) endemic in Chinese bat populations (Lau 2005). The phocine distemper virus (PDV) circulates among Arctic seal species, predominantly harp seals *(Phoca groenlandica),* ringed seals *(Phoca hispida)* and hooded seal *(Cystophora cristata)*, which can act as reservoirs from where new infections can spread to other seal species further south (Härkönen 2006).

Two of the most severe mass mortalities ever recorded in wildlife populations were caused by PDV epizootics in European harbour seals *(Phoca vitulina)* in 1988 and 2002, when more than 50,000 seals died (Härkönen *et al.* 2006). Mortality rate along mainland Europe was close to 50%, whereas British stocks were less affected on both occasions (Harding *et al.* in prep.).

The connectivity between source and peripheral host populations is one important parameter affecting the risk of transferring the infective

agent, but the potential future frequency of epizootics in European harbour seals is also limited by factors such as the virulence of the disease, and the proportion of population that is immune from previous outbreaks (Harding *et al.* in prep.). These factors will determine the time required to reach the critical herd immunity level (Anderson and May 1991) below which an epizootic will have a potential to expand. We discuss the different factors in the source population, in the vector, and in peripheral populations that can influence the risk for new outbreaks of the PDV among harbour seals in the North Sea area.

SOURCE POPULATIONS –ENDEMISM?

Emerging infectious diseases (EIDs) originate from species and populations where they have co-evolved with their host(s) (Grenfell and Dobson 1995). Such diseases can be maintained in source populations if the number of infectives resulting from an initially infected animal (R_0) in the very beginning of the epizootic, times the proportion susceptible (S) in the population, is equal to 1; thus R_0 *S=1 (Anderson and May 1991). The general pattern of very high R_0's for pathogens adapted to their hosts over a long time contrast with low R0's for pathogens crossing species boundaries (Lipsitch *et al.* 2003). Consequently, pathogens adapted to human populations generally show R_0's between 4 and 15 (Fig. 1), even though it can exceed 20 for epizootics caused by seasonal influenza viruses (Gog *et al.* 2003). Contrastingly, estimates of R_0 for EIDs such as SARS and Spanish flu vary between 1.5 and 4 (Fig 1, Lipsitch *et al.* 2003, Ferguson *et al.* 2006), where the ranges of estimates depend on different model assumptions (Nishiura 2007).

Under the assumption of a steady state, the R_0 can be readily estimated if the proportion of susceptibles is known for a specific endemic disease as *e.g.* for Canine Distemper Virus (CDV) in spotted hyenas (Harrison *et al.* 2004). However, repeated samples from the same population are required to verify that collected samples actually reflect a steady state.

In the case of the PDV, the feasibility of assuming a steady state can be investigated since serological data have been collected for Arctic seal species on several occasions in different

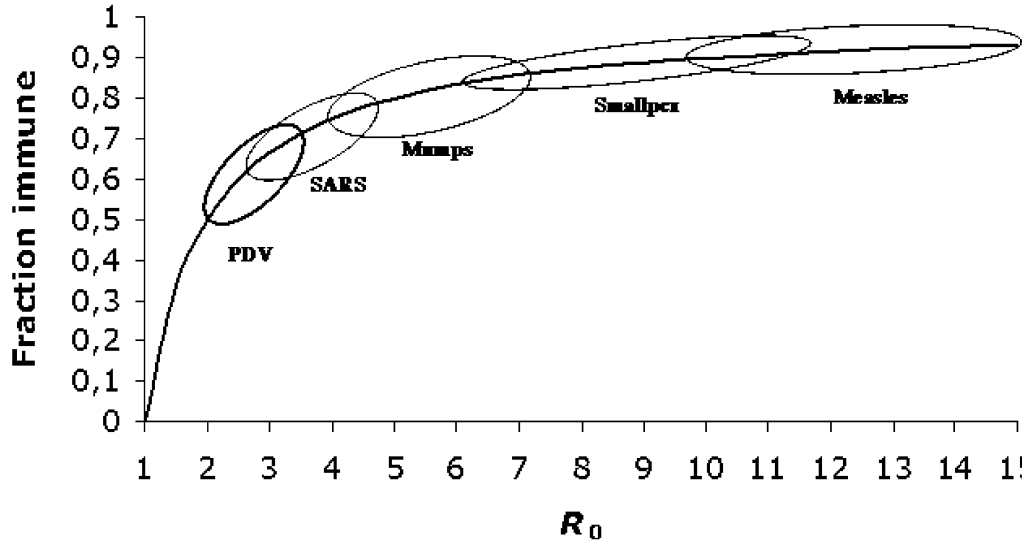

Fig. 1. *Herd immunity levels for some common human epidemic diseases as compared with emerging diseases such as SARS and the phocine distemper virus (PDV). The curve is given by the function $q_C = 1-(1/ R_0)$ (Anderson and May 1991), where q_C is the critical herd immunity level, and R_0 is the basic reproductive number.*

Table 1. Estimates of the basic reproductive number (R_0) of PDV in Arctic seal populations under a scenario where final fractions *(f)* affected by epizootics are reflected by the proportion seropositive in taken samples. In such a case the basic reproductive number is given by: $R_0 = - ln(1 - f)/f$ (Kermak and McKendrick 1927).

Species	Region	Year	n	Pos (%)	R_0	References
Harp seal	West Greenland	1985-86	40	30	1.19	Dietz *et al.* 1989a, b
Harp seal	Barents Sea	1987	10	10	1.05	Klingeborn 1990
Harp seal	Barents Sea	1987	28	0		Markussen and Have 1992
Harp seal	Barents Sea	1989	68	98.5	4.26	Klingeborn 1990
Harp seal	West Ice	1987	46	7	1.04	Markussen and Have 1992
Harp seal	West Ice	1987	37	97	3.62	Markussen and Have 1992
Harp seal	Canada	1971-80	10	30	1.19	Henderson *et al.* 1992
Harp seal	Canada	1988-93	157	83	2.13	Duignan *et al.*1997
Ringed seal	Greenland	1984-87	90	4	1.02	Dietz *et al.* 1989b
Ringed seal	NW Greenland	1988	10	0		Bohm *et al.* 1989
Ringed seal	E Greenland	1999-04	76	0		Kreutzer *et al.* 2007
Ringed seal	Svalbard	1986-87	29	0		Klingeborn 1990
Ringed seal	Canada	1972	3	67	1.65	Henderson *et al.* 1992
Ringed seal	Canada	1992-94	259	41	1.29	Duignan *et al.* 1997
Ringed seal	Alaska	1984-88	68	0		Osterhaus *et al.* 1988
Hooded seal	Canada	1983-84	11	2	1.01	Henderson *et al.*1992
Hooded seal	Canada	1989-94	185	24	1.32	Duignan *et al.* 1997

areas of their distribution. The proportion of populations seropositive to PDV has varied dramatically across years and among populations (Table 1). The seropositive proportion of harp seals in the Barents Sea has varied between zero and 98.5%, a pattern also seen in the West Ice, the area between Iceland and Greenland. This variation is also obvious in ringed seals and hooded seals (Table 1). Consequently, PDV is not circulating among Arctic seals according to the assumption of a steady state, but rather data indicate occasional outbreaks among the studied species and populations. A more appropriate method to estimate R_0 under such circumstances is given by:
(1)

$R_0 = - ln(1 - f)/f$ (Kermack and McKendrick 1927),

where *f* is the fraction finally affected in a naïve population.

If immunity from previous infections is negligible, the highest estimates of R_0 could be close to actual values if the samples were taken just after the epizootic outbreak. The highest estimates of R_0 for PDV among harp seals in the West Ice and Barents Sea range between 3.62 and 4.26, where 97% and 98.5% of sampled seals were seropositive to PDV (Table 1).

Serological data (*e.g.* Thompson *et al.* 2002) and age structure analysis from repeated epizootics (Härkönen *et al.* 2007) indicate that seals exposed to PDV become immune for life, whereas cohorts born after epizootic years are susceptible (Thompson *et al.* 2002, Härkönen *et al.* 2007). Thus, serological samples taken several years after a PDV epizootic may more reflect the proportion of a population born after an epizootic, than the virulence of the virus itself. This is likely the reason for many of the low estimates of R_0 given in Table 1. Nevertheless, the data in Table 1 show that PDV has been circulating among at least 3 Arctic seal species, and that different populations were affected in different time periods.

CARRIER SPECIES AND PERIPHERAL POPULATIONS

Massive migrations of starving harp seals from the Barents Sea to the Norwegian coast occurred in the winter and spring before the 1988 harbour seal epizootic (Haug *et al.* 1991). Harp seals were also reported from the North Sea area, and it was suggested that harp seals brought the PDV to the North Sea harbour seals (Heide-Jørgensen and Härkönen. 1992). Since no such migrations preceded the 2002 outbreak, the route of infection cannot be explained by harp seals on this occasion.

Scanning of potential carrier species in the North Sea area has to date only identified grey seals as carriers of the PDV (Härkönen *et al.* 2006), whereas tested samples from polar bears *(Ursus maritimus)* and mink *(Mustela vison)* proved negative for morbillivirus infection (Kreutzer *et al.* 2007).

The situation in the West Atlantic is somewhat different. Samples from grey seals and harbour seals collected since the beginning of the 1980s show antibodies against PDV with a prevalence ranging between 33 to 83% (Table 2), but there is also evidence for infected polar bears in the Canadian Arctic (Cattet *et al.* 2004, Philippa *et al.* 2004). This pattern suggests that West Atlantic populations of seals have been exposed to PDV over a longer time scale than in the North Sea area, and that they have been exposed more frequently.

VULNERABILITY TO RECURRING INFECTIONS IN NORTH SEA HARBOUR SEALS POPULATIONS

The PDV is obviously capable of infecting many species of seals and at least one semi terrestrial mammal, the polar bear (Tables 1

Table 2. Indications of exposure to PDV infection in seal populations at temperate latitudes.

Species	Region	Year	n	Pos (%)	References
Grey seal	Canada	1980-81	9	33	Henderson *et al.* 1992
Grey seal	Canada	1989	24	63	Carter *et al.* 1992
Grey seal	NE USA	1980-94	296	73	Duignan *et al.* 1995
Grey seal	UK	1985-87	90	0	Harwood *et al.* 1989
Grey seal	England	1988	16	0	Carter *et al.* 1992
Grey seal	Scotland	1988	12	0	Klingeborn 1990
Grey seal	UK	1989	45	96	Cornwell *et al.*1992
Grey seal	Wadden Sea	1989-91	41	0	Kreutzer *et al.* 2007
Grey seal	Baltic	1981-89	30	0	Klingeborn 1990
Grey seal	Baltic	1990	1	100	Klingeborn 1990
Harbour seal	E Canada	1989	11	36	Carter *et al.* 1992
Harbour seal	NE USA	1980-94	387	37	Duignan *et al.*1995
Harbour seal	NE USA	1991-92	36	83	Duignan *et al.* 1995
Harbour seal	North Sea	1984-88	134	0	Osterhaus *et al.* 1988, 1989
Harbour seal	N Baltic	1983-87	10	0	Klingeborn 1990
Harbour seal	N Baltic	1988-89	14	0	Klingeborn 1990
Harbour seal	England	1988	32	63	Carter *et al.* 1992
Harbour seal	England	1989	28	11	Carter *et al.* 1992
Harbour seal	England	1990	14	0	Carter *et al.*1992
Harbour seal	UK	1989	56	55	Harwood *et al.* 1989

and 2, Cattet *et al.* 2004). Thus, cross-species infections appear to be common, and may be the reason why it is maintained in Arctic populations, since the persistence population level for PDV is much greater than the size of any single seal species in the Arctic (Swinton *et al.* 1998). Thus, genetic properties of the PDV do not seem to put severe limitations for crossing species barriers. The risk for future outbreaks of PDV epizootics in the North Sea area is therefore likely determined by the connectivity between source populations in the Arctic and harbour seal populations further south, and the susceptibility of seal populations in the North Sea area.

CONNECTIVITY

Since exposure to PDV results in life-long immunity (Härkönen *et al.* 2007), serum samples taken before 1988 provide one clue to the frequency of exposure to PDV in the North Sea. All samples from harbour seals and grey seals taken prior to 1988 proved negative to PDV, indicating that seals hadn't been exposed to the virus for at least two-three decades. Further, age structure analysis of the seals that died in the 1988 epizootic showed that the mortality rate in the oldest age class (25-34 years of age), was similar or greater than expected as compared with the age structure of affected populations (Härkönen *et al.* 2007). These combined data sets strongly indicate that PDV epizootics had not occurred in the North Sea area at least since the late 1950s. However, mass mortalities among seals have been recorded in the 19th century in British waters (Harwood *et al.* 1989), and also in Iceland in 1918 (Bardarson 1933), where many seals died of symptoms similar to those seen in victims of the 1988 PDV epizootic (Bergman *et al.* 1990). It is therefore suggested that PDV epizootics in the North Sea area could have occurred occasionally over the past centuries, but if so, at long intervals.

MECHANISMS OF TRANSMISSION

One outstanding fact is that both the 1988 and 2002 PDV epizootics started at the island of Anholt in central Kattegat, from where it spread

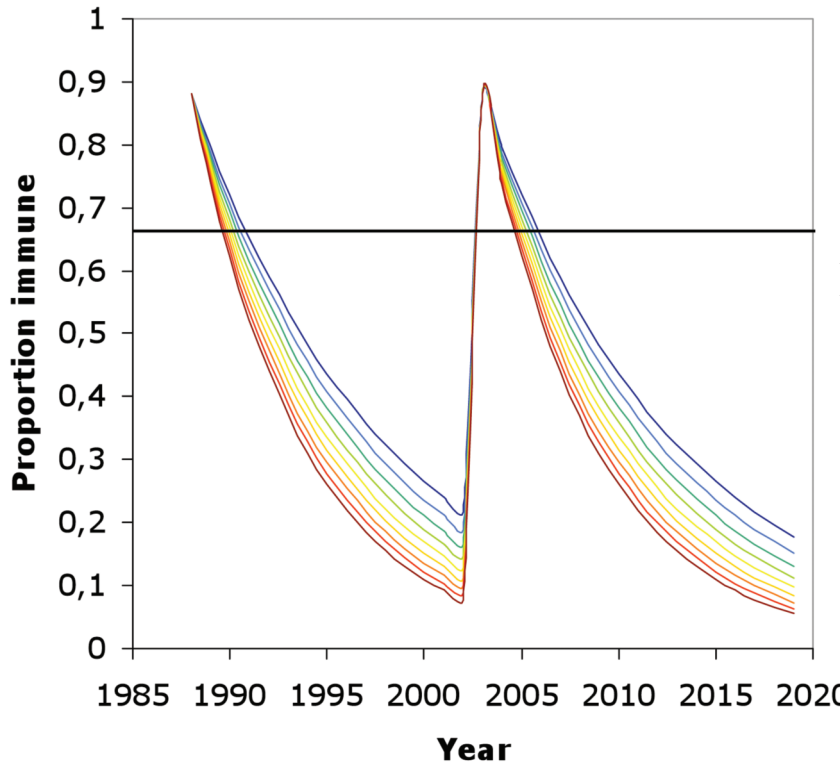

Fig. 2. *Proportions of populations immune to phocine distemper after the 1988 and 2002 PDV epidemics. Horizontal line denote the critical herd immunity level (0.67) at R_0= 3.0. Curved lines show population along Mainland Europe where growth rates (l) have varied between 1.06 (blue) and 1.13 (red).*

in a stepwise fashion to most European harbour seal populations (Härkönen *et al.* 2006). Since there are more than 100 haulout sites in the North Sea area, the probability for a repeated initial infection at the same site would be less than 1% if the transmissions occurred as random events. So why did both epizootics start at Anholt island?

More detailed analyses of the propagation of both epizootics show that even though they mainly spread to neighbouring colonies, sudden jumps to distant regions occurred both in 1988 and 2002 (Härkönen *et al.* 2006). In 1988 the infection jumped to the Irish Sea before it hit adjacent infected colonies, and in 2002 the plague appeared in the Netherlands before the northern parts of the Wadden Sea. Such sudden jumps coincide with the occurrence of grey seal colonies in those regions. Since grey seals also occur at Anholt island, both the jumps in dispersal of the epizootics and the initial outbreaks at Anholt would be explained by the fact that grey seals could act as carriers of PDV between Arctic and North Sea populations on the one hand and among seal colonies in the North Sea area on the other. However, although these patterns can be taken as circumstantial evidence that grey seals played a key role in the outbreaks, this hypothesis is still to be proven by data to be collected on grey seals along the Norwegian coast.

LAG PHASES AND HERD IMMUNITY LEVELS

The success of an infective agent with R0>1, will partly depend on chance events in the beginning of an epizootic, when numbers of infected hosts are few (Heide-Jorgensen and Härkönen 1992), which could lead to lag-phases of varying lengths of time, or fade-outs in totally susceptible (pristine) populations. This could be seen during the 1988 epizootic where the first recorded positive cases at some sites occurred many weeks before the exponential phase of the epizootic started (Dietz *et al.* 1989a, b).

The possibility for new epizootics to expand in a previously exposed population depends on the basic reproductive number (R_0), and the proportion that is susceptible in the population. Following Anderson and May (1991), we define the critical herd immunity level (q_c) as:
(2)

$$q_c = 1-(1/ R_0)$$

where $q_c = 1-S$.

Given that R_0=3.0 (Harding *et al.* in prep.) for PDV, q_c = 0.67. Since cohorts born after an epizootic lack acquired immunity to PDV, the proportion susceptible to a new infection will increase with time as function of population growth rate and mortality rate.

As mentioned above, the final size of an epizootic in a naïve population is given by: $R_0 = - ln(1 - f)/f$ (Kermak and McKendrick 1927). Thus, at R_0=3.0, about 94% of harbour seals were exposed to the 1988 and 2002 PDV epizootics. Consequently, since mortality was about 50% on both occasions, the proportion immune among survivors would be about 88% just after the epizootic. The proportion immune will change with time due to natural mortality on the one hand and births of new susceptible cohorts on the other.

We set the natural annual mortality at 0.05 (Härkönen and Heide-Jorgensen 1990) and estimate the change in proportion of susceptibles (S) in populations of harbour seals. The annual decrease in numbers of immune *(Q)* is given by: Q_x+1= Q_x*0.95, and the change in the size of the total population from one year to the next is given by: N_{x+1}= N_x*λ, where N_x is the total population size in year x, and λ the annual net growth rate. Given that q_x = 0.88 when x=0, the proportion immune over time will decrease according to:
(3)

$$q_{x+1}= 0.88N_x*0.95/ N_x*\lambda$$

Populations of harbour seals along mainland Europe showed annual growth rates (λ) ranging between 1.05 (Baltic) and 1.13 (Skagerrak and Wadden Sea) after the 1988 epizootic. The proportion immune decreased below the herd immunity level at 0.67 in years 1991-1993 in different populations. All populations were thus open for new epizootics only after 5 years. However, it took 14 years until the new

epizootic emerged in 2002, when the proportion immune varied between approximately 0.1 and 0.3 among populations. Both these epizootics caused about 50% mortality in populations along mainland Europe, but mortality rates were lower in the Baltic and the Kattegat, where population growth rates were lower compared with other populations.

Populations along mainland Europe recovered after the 2002 epizootic at similar annual growth rates as after the first epizootic, and the proportion immune predicted has passed the critical herd immunity level in 2005 to 2007. Consequently, all populations of harbour seals are currently below the herd immunity level, and are thus vulnerable for new outbreaks.

CONCLUSIONS

PDV has been circulating for a long time in several species of Arctic seals and also infects polar bears in the Canadian Arctic. Grey seals and harbour seals in the West Atlantic have been infected many times over the past decades, but no mass mortalities caused by PDV have ever been observed along the North American east coast. The grey seal is the only identified species that could act as carrier of PDV between Arctic and North Sea seal populations, and grey seals are also suggested to have contributed to the spread of the virus both in the 1988 and 2002 epizootics. However, successful introductions of PDV appear to be relatively rare, since they have only occurred twice over the past century. The maximum frequency of PDV epizootics is determined by herd immunity levels of populations. Since seals exposed to PDV attain lifelong immunity, the proportion immune in the population will decrease as a function of mortality rate, and birth rates of new susceptible cohorts. Populations of harbour seals along mainland Europe were below herd immunity levels 4-5 years after both the 1988 and 2002 epizootics, and future outbreaks of PDV are pending.

ACKNOWLEDGEMENTS

We thank the Swedish Environmental Protection Agency for supporting the study financially. K.C. Harding was funded by the Centre for Theoretical Biology, University of Gothenburg.

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