Assessment of the productivity effects associated with epizootic hemorrhagic disease in dairy herds

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ABSTRACT

Epizootic hemorrhagic disease is caused by a *Culicoides*-borne *Orbivirus*. In cattle, the disease is characterized by reduced milk production and mortality. Recent outbreaks of epizootic hemorrhagic disease virus (EHDV) in North Africa, Israel, and Turkey increase the risk of its invasion into central and northern Europe. An outbreak of EHDV in Israel during the fall of 2006 enabled an assessment of the consequent production losses to the dairy cattle industry. Reduction in milk production and involuntary culling were modeled using a 4-yr database of monthly milk and mortality records from 48 affected and 63 unaffected herds. These indices were compared between periods of outbreak and no outbreak and assessed for various levels and exposure onset. Geospatial kriging interpolation of serological results from 127 herds was used to assess the total outbreak losses for the dairy cattle industry in Israel. Herds affected during the first, second, and third month of the outbreak (September–November) experienced an average loss of 207 (95% CI = 154–261), 137 (63–211), and 52 (27–76) kg of milk/milking cow, respectively, during the outbreak period. An average excess mortality and involuntary culling of 1.47/100 cows was documented in herds affected in September. High correlation was observed between EHDV seroprevalence and milk loss; average milk loss for herds with seropositivity of 26 to 50, 51 to 75, and 76 to 100% was 84, 133, and 204 kg of milk/milking cow, respectively. A 1.42% (0.91–1.93%) increase in mortality was observed in herds with seroprevalence above 50%. Losses for the dairy cattle industry interpolated from these data were estimated at US\$2,491,000 (US\$1,591,000–3,391,000), an average loss of US\$26.5/cow in the Israeli dairy cattle. This equals 0.55% of the average total value production of a dairy cow in Israel. This is the first study to estimate the production losses caused by EHDV or any bluetongue-like disease.

Key words: epizootic hemorrhagic disease, economic loss, bluetongue, milk loss

INTRODUCTION

Epizootic hemorrhagic disease virus (EHDV) is an arthropod-borne, double-stranded RNA virus of the genus *Orbivirus* (Fenner et al., 1974). It is traditionally regarded as the causative agent of fatal hemorrhagic disease in white-tailed deer (*Odocoileus virginianus*) (Karstad et al., 1961), but other domestic and wild ruminants may also be infected (Jessup, 1985; Pearson et al., 1985). Until recently, it was believed that EHDV does not usually cause significant clinical signs in cattle (Uren, 1986; Bowen, 1987; Aradaib et al., 1994; Abdy et al., 1999) apart of the ibaraki virus, which is closely related to EHDV serotype 2 (Iwata et al., 2001) and has caused several outbreaks in Japan and Korea in which thousands of head of cattle were affected (Kitano, 2004). However, recently, outbreaks of EHDV in dairy cattle were reported from the island of Reunion (Bréard et al., 2004), Israel (Yadin et al., 2008), Morocco and Algeria (ProMed archive numbers 20061010.2906, 20061214.3513; <http://www.promedmail.org>), and Turkey (Temizel et al., 2009). The latter 3 outbreaks were caused by EHDV serotype 6. A reassortant strain with this particular serotype was recently isolated from Indiana, Illinois, Missouri, Kansas, and Texas (Allison et al., 2009). This was parallel to EHDV-associated cattle morbidity that was reported from Kentucky and Ohio on 2007 (ProMed archive numbers 20070905.2922, 20070928.3208 for Ohio and Kentucky, respectively). Thus, EHDV causes morbidity in dairy cattle in the United States, but its economic impact was never quantified.

In September 2006, an outbreak of EHDV occurred in Israel (Yadin et al., 2008). The disease was reported in 83 dairy herds (average 380 cows/herd) and 22 beef herds. The outbreak was first noticed on several dairy farms in the southern Jordan Valley in Israel (part of the Rift Valley) and it spread to the northern, southern, and western parts of Israel. Anorexia, followed by reduced rumination, a short-term low fever, weakness,

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and stiff gait were observed in many cows together with a variety of other clinical signs. However, the most consistent clinical sign was reduced milk production. Low mortality was also observed. These 2 latter characteristics are the main reasons for economic losses because of EHDV infection.

The appearance of EHDV in Turkey in 2007 demonstrates the potential for its spread into Europe (Temizel et al., 2009). This potential and the finding of new cattle-virulent EHDV incursion in the United States (Allison et al., 2009) emphasize the need for adequate assessment of the potential production losses it can cause. The aim of this study was therefore to assess the production losses caused by milk loss and mortality associated with EHDV infection.

MATERIALS AND METHODS

Study Population

Cow milk in Israel is produced under a quota system. The herds are divided mainly into 2 types: herds in cooperative farms (kibbutz) and family herds. In 2006, 57% of the milk was produced on cooperative farms, on which herd size averaged 364 cows. The other 42% was produced in family herds, of which 75% are members of the Israeli Cattle Breeders Association (ICBA; Caesarea, Israel) and take regular monthly milk recordings. Average size of these herds was 65 cows. Another 1% was produced by agriculture school farms. In the herds of cooperative farms, cows are milked 3 times daily and their average annual milk production per cow during 2006 was 11,744 kg. In most of the family herds, cows are milked twice daily and the average milk production per cow during 2006 was 10,508 kg. The study included 111 herds of high-producing Israeli Holstein cows held under zero grazing in free-stall sheds. Of these, 101 were herds of cooperative farms and 10 were family herds. All of these herds were members of the ICBA, in which monthly milk recordings were performed. The herds were categorized according to either EHDV seroprevalence or clinical presentation. Herds that reported typical EHDV clinical signs were included in the analysis as clinically affected ($n = 48$). Herds that did not report typical clinical signs were included as controls ($n = 63$).

Assessment of Exposure to EHDV

Serum samples were collected from affected herds at least 1 mo after the appearance of clinical signs. Control herds were sampled in November and December, during the final stages of the outbreak. Overall, 127 herds were sampled. Monthly milk recordings were taken on

a regular basis from 119 of these 127 herds. Of these 119 herds, 3 were affected by another severe disease during the period between 2005 and 2008 (lumpy skin disease) and were therefore omitted from analysis. Five other herds were merged during this period and were omitted also from analysis. Therefore, 16 herds (11 affected and 5 unaffected) were sampled serologically but were not included in the analysis. This left 111 herds to be included in the study. Veterinarians were instructed to collect the following serum samples from each case herd: 5 samples were collected from calves aged 6 to 12 mo, 5 from apparently healthy cows, 5 from cows that had begun showing clinical signs (including reduced milk production) at least 2 wk before blood sample collection, and 5 samples from cows that were sick during collection. In the control herds, serum samples were collected only from calves and healthy cows. The sample size rationale favored sampling from a wide geographical distribution over collection of a high number of samples from a smaller number of herds. According to this sampling strategy, the probability of missing infection in a herd in which 20% of the cows are affected was calculated to be 10%. For a 30% affected herd, this probability was less than 3%.

A competitive ELISA similar to an assay previously presented by Thevasagayam et al. (1996) was used to identify the presence of antibodies against EHDV in the serum samples. This ELISA was previously shown to have no cross-reaction with Bluetongue virus (BTV) and to detect exposure to all serotypes of EHDV. Specificity and sensitivity of this assay were shown to be 100% (as compared with agar immunodiffusion test; Thevasagayam et al., 1996). Briefly, the EHDV competitive ELISA was performed as follows: EHDV-1, purified as described previously (Thevasagayam et al., 1995), was incubated at a dilution of 1:250 at 37°C for 1 h on an orbital shaker. The plates were washed 3 times before loading of the test serum samples, control sera, and competing monoclonal antibody (EHDV VP7-specific, at a dilution of 1:100). Four wells were loaded with all reagents but no sera and were considered zero-competition controls. After incubation (1 h, 37°C), the conjugate (Dako rabbit anti-mouse horseradish peroxidase; 1:1,000) was added and the plate was incubated for 1 h at 37°C. The substrate (Zymed TMB single solution, Zymed Laboratories Inc., San Francisco, CA) was added and after incubation (15 min), the reaction was stopped by the addition of 1 M sulfuric acid. The plates were read at 405 nm (ELISA reader SUNRISE, XFLUOR4 version V4.51, Tecan Austria GmbH, Salzburg, Austria). Optical density (OD) values were converted to percentage inhibition values, which were calculated as follows: $100 - (\text{OD of each test or control value} / \text{median OD of the 4 wells})$

× 100. Percentage inhibition values of 50% or greater were considered positive.

Milk Production and Mortality Data Collection

Monthly milk records were provided by the ICBA for each cow for the period between January 2005 and July 2008. Milk records from cows that were below 5 or above 305 DIM were excluded. Overall 1,521,247 monthly milk records were analyzed in the study. Cases of sudden death or euthanasia (**SDE**) and cases of salvage slaughter are routinely recorded in the herd-management software (NOA, Israel Cattle Breeders Association), each given a separate code. For most of this study, they were merged into one category defined as involuntary culling (**IC**). For the purpose of comparison and validation of the analyzed database, data on SDE were also collected from the Israeli Central Facility for Corpse Disposal (**ICFCD**; Ein-Hamifratz, Israel). According to Israeli law, all corpses of cattle dying in a herd must be disposed of at this facility. The assumed diagnosis is reported on the death certificate by the practitioners attending the herds and recorded in the facility database.

Data Analysis

The initial analysis was performed to calculate an adjusted average of milk production for each herd during each month. This was performed by using PROC GLM of SAS (SAS Institute, Cary, NC). The initial general linear model for calculating an adjusted milk record (Y_{ijkm}) was

$$Y_{ijkm} = H_i + M_j + H_i \times M_j + PAR_k + DIM_m + DIM_m^2 + DIM_m^3 + PAR_k \times DIM_m + PAR_k \times DIM_m^2 + PAR_k \times DIM_m^3 + e_{ijkm},$$

where H_i (111 index variables) is the effect of herd i ; M_j (43 index variables) is the effect of month j ; PAR_k (3 index variables: 1, 2, 3+) is the effect of parity k ; DIM_m is the effect of day m in milk; and e_{ijkm} is the residual random error for a milk record taken during month j from a cow from herd i that is in the m th DIM and parity k . The command LSMEANS of SAS (SAS Institute) for the interaction $H \times M$ was then used to calculate the average adjusted milk production for each herd in each month from January 2005 to July 2008.

Average adjusted milk production for each herd during each month was used in the second phase of analysis. This analysis was performed to estimate milk loss according to month of outbreak onset (September, Oc-

tober, or November) and stages of the outbreak within each herd. For this analysis, the 6 mo following outbreak onset were coded according to the specific month in which clinical signs were first reported. For example, if an outbreak in a certain herd began in September, month of onset for all 6 mo from September to February were coded as 9. Analysis of IC was performed by the same methodology.

Another analysis was performed to associate level of EHDV seroprevalence with milk loss and increased IC. This was performed to calculate milk loss and mortality for all of Israel. Because date of outbreak onset was not reported from all seropositive herds, we used the results from the first stage of the analysis to decide on the period of significant milk loss for the entire Israeli epizootic. The seroprevalence was coded other than 0 only for this period. Herds were classified into 5 groups according to seroprevalence of EHDV (0, 1–25, 26–50, 51–75, and 76–100%). Increase in IC was calculated for the entire period for which EHDV-associated deaths were reported at the ICFCD. For those months, all the seropositive herds were coded according to seropositivity level, whereas the rest of the time they were coded as 0.

Data were correlated at the herd level. Therefore, analysis of milk loss and IC was performed using a generalized estimating equations regression model (SPSS Inc., Chicago, IL) with an exchangeable covariance structure for the working matrix (i.e., correlation between milk measurements and IC within the herd but not between the herds). Month, year, and month of outbreak onset were defined as fixed variables. The Wald chi-squared statistic was used to compute statistical significance of the parameter estimates. To estimate losses according to month of outbreak onset and stage of outbreak within each herd, we included all main effects in the model as well as the interaction between month and month of outbreak onset. The following model was used to calculate the average daily milk production (Y) for a certain month in a certain year:

$$Y = M + Yr + MONST + MONST \times M + e,$$

where M (12 index variables) is the month, Yr (4 index variables) is the year, and $MONST$ (4 index variables including 0) is the month of onset of outbreak in each herd. The model marginal means for each month in each month of onset were then retrieved. For estimation of total losses in herds according to month of onset, we used a model that included only the main effects, where the month of onset variable was coded only for the period in which significant milk losses or IC were recorded.

For estimation of the association between milk loss or IC and EHDV seroprevalence, we used the following model:

$$Y = M + Yr + EHDV + Htype + e,$$

where *EHDV* (5 index variables) is the EHDV seroprevalence effect with 5 categories and *Htype* (2 index variables) is the herd type (cooperative or family herd). If main effect for *Htype* was statistically significant, its interaction with *EHDV* was added to the model. If this was also significant, the model was calculated separately for family and cooperative farms.

To estimate the losses for the entire dairy cattle industry in Israel, we used a spatially based approach. We first performed a Logit-transformation of the seroprevalence data after subtracting or adding 4% from the points with 100 and 0% seroprevalence, respectively. We used kriging to interpolate the logit-transformed serological results from the survey data to the entire country. This was performed by using the Geostatistical Analyst extension of ArcView 9.3 software (ESRI Inc., Redlands, CA). Kriging is a statistical interpolation method that uses data from a single data type (single attribute) to predict (interpolate) values of that same data type at unsampled locations. It produces an estimate of the underlying (usually assumed to be smooth) surface by a weighted average of the data, with weights declining with distance between the point at which the surface is being estimated and the locations of the data points. The exact nature of the decline is based on modeling the covariation between data at various spatial locations. This model is called a semivariogram (Johnston et al., 2001). Kriging interpolation was performed by using a few optional semivariogram models—circular, exponential, Gaussian, and spherical. Coefficient of determination for the association of the estimates generated by cross-validation with real data was then calculated to determine goodness of model fit. Using this procedure, we decided to use the most parsimonious spherical model for which coefficient of determination was 0.7. The resultant interpolated geographical information system (GIS) layer and the standard error layer of the estimates were joined, based on spatial location, with a layer depicting the dairy herds in Israel (kindly provided by the ICBA). Milk loss and increased IC were estimated for each farm based on its interpolated seroprevalence. Losses were calculated based on the size of the herd, its estimated milk loss per milking cow, and percentage of IC increase.

Confidence intervals were calculated using Excel (Microsoft, Redmond, WA) by repeated Monte Carlo simulations of the herds' logit-transformed seropreva-

lence, assuming normal distribution with the mean and standard error deduced from the interpolation model. This set of simulated herd seroprevalence was then multiplied by simulated losses for each EHDV seroprevalence category, for which the mean and standard error were estimated by the generalized estimating equations model. These simulations were repeated 10,000 times to estimate the variance for total milk loss and increased IC.

The value of production losses were calculated according to the agreed-upon national prices published by the ICBA. The basic price (target price) of milk results from a triple agreement between government, farmers, and dairy plants regarding the monthly price that the industry should pay for the raw milk produced and collected each month. In September 2006, the milk target price was (prices in US dollars) \$0.38/kg. The SDE loss equals the average value of a cow, \$1,245, which is the midpoint between heifer replacement cost of \$1,650 and its normal cull value of \$840. For salvage slaughter, we subtracted the meat price, which was very low because of the cows' condition: \$100 on average. Therefore, a loss value of \$1,145/cow was calculated for a case of salvage slaughter. These losses were compared with the average total value production produced by a dairy cow in the Israeli herd, which was \$4,865. This value was calculated by adding the average value of milk production per cow (11,281 kg × \$0.38) to the average annual number of calvings per cow multiplied by the value of 1-wk-old calf (1.025 × \$287) and to the average cull value (\$840) multiplied by the cull percentage in 2006 (33.8%). The same method was used to calculate a specific average value production of \$5,040 and \$4,571 produced by a dairy cow in cooperative and family herds, respectively.

RESULTS

Comparison of Herd Basic Characteristics

Affected herds analyzed included a significantly higher percentage of cooperative farms when compared with the affected herds that were not included in the study. This resulted in a significant difference in the number of cows between the 2 groups. However, there was no statistically significant difference between the 2 groups in milk production, total cull, SCC, and EHDV seroprevalence (Table 1). Performance of these comparisons separately for cooperative and family farms showed no statistically significant difference between the herds included and not included in the study.

There was no statistically significant difference in herd size, total cull, and SCC between affected and nonaffected herds (Table 1). Annual average milk pro-

Table 1. Comparison between sampled case herds, nonsampled case herds, and sampled control herds¹

Item	Affected herds	Unaffected ² herds	Affected herds not included in the study	<i>P</i> -value ³
Herds (n)				
Cooperative	40	61	12	<0.0001
Family	8	2	23	<0.0001
All	48 ^a	63 ^b	35 ^c	<0.0001
Herd size (n)				
Cooperative	342 (157) ^a	378 (183) ^a	391 (208) ^a	0.58
Family	83 (37) ^{ab}	118 (45) ^a	70 (27) ^b	0.095
All	300 (174) ^a	370 (185) ^a	174 (192) ^b	<0.0001
Annual milk production (kg/cow)				
Cooperative	11,426 (694) ^a	12,022 (769) ^b	11,701 (707) ^a	0.001
Family	10,964 (527) ^a	10,866 (1,178) ^a	11,024 (670) ^a	0.935
All	11,350 (686) ^a	11,985 (799) ^b	11,243 (744) ^a	<0.0001
Cull during 2006 (%)				
Cooperative	32 (7.3) ^a	34 (6.2) ^a	32 (6.7) ^a	0.501
Family	26 (7.5) ^a	35 (1.4) ^a	26 (9.3) ^a	0.394
All	31 (7.6) ^{ab}	34 (6) ^a	28 (8.9) ^b	0.002
SCC ($\times 10^3$)				
Cooperative	186 (39) ^a	198 (88) ^a	187 (28) ^a	0.665
Family	172 (45) ^a	295 (147) ^b	190 (56) ^a	0.043
All	184 (40) ^a	201 (90) ^a	189 (48) ^a	0.382
EHDV seroprevalence ⁴				
Cooperative	70 (26) ^a	8 (13) ^b	85 (9) ^a	<0.0001
Family	52 (33) ^{ab}	6 (9) ^a	59 (32) ^b	0.133
All	68 (27) ^a	8 (13) ^b	64 (31) ^a	<0.0001

^{a-c}Means within a row with different superscripts are statistically different ($P < 0.05$; calculated by independent sample *t*-test).

¹Values are average (SD).

²According to clinical report by the veterinarians.

³Calculated by one-way ANOVA.

⁴EHDV = epizootic hemorrhagic disease virus.

duction per cow in the affected herds, however, was 635 kg less than in the nonaffected herds. This difference was also apparent when only cooperative farms were compared. As expected, there was a significant difference in EHDV seropositivity between these 2 groups. Furthermore, only 39% of the control herds showed some level of EHDV seroprevalence as opposed to the clinically affected herds, which were all seropositive.

Association of Losses with Time of Outbreak Onset

Milk loss during the epizootic was associated with the time of outbreak onset and time elapsed since outbreak onset. Herds affected during the early stage of the epizootic, in September, showed a significant reduction in milk during the 4 mo following outbreak onset, whereas herds affected in October and November showed 3 and 2 mo duration of milk loss, respectively (Figure 1). Overall, an average reduction of 207 (95% CI = 154–261), 137 (63–211), and 52 (27–76) kg of milk/milking cow was observed in herds in which outbreaks began in September, October, and November, 2006, respectively (Figure 2).

Involuntary culling increased significantly only in herds affected in September, during the 2 first mo of

the outbreak (Figure 3). Overall, an increase of 1.47% (0.95–1.82) was calculated in these herds.

Association of Losses with EHDV Seroprevalence

Based on the initial analysis, it was concluded that significant milk losses occurred for a period of 4 mo between September and December, whereas a significant increase in IC was documented in September and October. However, analysis of the ICFCDB database shows that mortality attributable to EHDV occurred between September and December (Figure 4). We therefore calculated milk loss and IC increase associated with serological results for the period of September to December 2006.

Overall, the average milk losses for herds that showed EHDV seroprevalence of 1 to 25, 26 to 50, 51 to 75, and 76 to 100% were 4 (–54 to 62), 84 (30–138), 133 (7–259), and 204 (150–258) kg of milk/milking cow, respectively. Because the main effect of herd type and its interaction with EHDV seroprevalence category were statistically significant, these figures were also calculated separately for cooperative and family herds. This analysis revealed similar trends in both family and cooperative herds, though in the former, estimated losses were smaller

Figure 1. Average monthly milk loss (kg/milking cow per day) for the period from outbreak onset until February 2007. Separate graphs are presented for herds affected in September, October, and November. Whiskers represent confidence intervals.

and had wide confidence intervals and were therefore statistically insignificant (Figure 5).

There was no statistically significant association between herd type (family or cooperative) and IC percentage ($P = 0.986$). This term was therefore excluded from the model. Herds with EHDV seroprevalence of 51 to 75 and 76 to 100% showed an average increase of 1.63 and 1.29% IC, respectively, whereas no such increase was apparent in herds with EHDV seroprevalence lower than 50% (Figure 6). We therefore combined the categories and calculated an IC increase of 1.42% (0.91–1.93%) in herds with an EHDV seroprevalence of over 50%. Increase of SDE in these herds was 1.17% (0.75–1.61%), accounting for 83% of the IC cases.

Estimation of Losses Caused by the EHDV Outbreak in 2006

Based on interpolation results, Israel could be divided into roughly 4 risk zones (Figure 7). Approximately 37,600 milking cows were located in risk zones with an average EHDV seroprevalence of greater than 25%. The simulation results indicate that an additional 5,000 cows located outside of these zones might have been exposed to EHDV during the outbreak. Together, this accounts for approximately 45% of the Israeli dairy herd. Using these figures, we estimate a total production loss of 5,333,000 (2,979,000–7,689,000) kg of milk because of the outbreak and 378 (250–506) cases of IC for all of the dairy cattle in Israel (Table 2). Our previous analysis indicated that 83% of these cases can be attributed to SDE; therefore, we estimate that 314 (208–420) cows died or were euthanized in the herd. Analysis of the ICFCD database indicates that 216 cow corpses, reported by the practitioners to have died as a result of EHDV, were disposed of at the central disposal facility between September and December. The overall milk losses and increased IC are summed to an estimated total loss of \$2,491,000 (\$1,591,000–3,391,000). Dividing this figure by the total number of dairy cows in Israel, we calculated a national loss of \$26.5/dairy cow. This equals a loss of 0.55% of the total annual production of an average cow in the Israeli dairy herd and of 0.53 and 0.58% for the average cow in cooperative and family farms, respectively. Losses in highly affected herds are estimated at \$95, which equals 1.95% of the total annual production of an average cow in the Israeli dairy herd.

DISCUSSION

To the best of our knowledge, this study provides the most comprehensive analysis of milk loss and mortality in dairy cattle as a result of cattle-virulent EHDV or BTV. Our analysis shows that EHDV outbreaks may result in significant economic losses because of loss of milk and increased fatalities. According to the estimates for the severely affected cooperative dairy herds, in which seropositivity was close to 100%, a loss of \$95 per cow can be attributed to EHDV infection, which equals 2% of the total annual production of these cows. This is a significant loss even when compared with the most costly production diseases in the dairy herd. For example, a recent review summarized an average estimated loss of 345 kg/lactation for a clinical case of mastitis in a Holstein cow (Seegers et al., 2003). For periparturient diseases like dystocia, stillbirth, milk fever, retained placenta, metritis, cystic ovaries, ketosis, and displaced abomasum, reduction in milk production

Figure 2. Average milk loss (kg/milking cow) for the total outbreak period for herds affected in September, October, and November. Whiskers represent 95% confidence intervals.

was estimated to range between 0.3 and 3.3 kg/d for a lactation period (Fourichon et al., 1999). Losses caused by EHDV can be also compared with losses caused by other infectious diseases. Reduction in milk production because of Johne's disease was estimated to be 15 to 19.5% during the lactation in the year of culling for clinically affected cows, but no such reduction was observed for previous lactations (Benedictus et al., 1987; VanLeeuwen et al., 2001). There is a controversy as to reduction in milk production caused by infection with other agents like *Neospora caninum* (ranging from 340 to no loss in production) or enzootic bovine leukosis (ranging from 218 kg/cow in infected herds to no losses; Chi et al., 2002; Ott et al., 2003). The average milk loss estimated in this study per clinical case of EHDV was 204 kg. Unlike the above mentioned conditions, incidence of infection with EHDV during an outbreak can reach 100% in many herds. It can therefore be recognized that during such periods, losses caused by of EHDV are the most costly in the dairy herd. However, as opposed to enzootic diseases, losses caused by infection by viruses like EHDV or BTV are highest when they are first introduced or when they reemerge, a situation that is difficult to predict. An outbreak of EHDV, for example, did not reoccur in Israel since 2006, as opposed to bovine ephemeral fever, which is another arthropod-borne virus that reemerges in Israel every few years.

Despite the huge outbreak of BTV-8 experienced by Europe in recent years, data on milk loss and mortality in dairy cattle caused by BTV or EHDV are scarce. A detailed analysis of losses caused by BTV-8 that was recently published attributed the most significant portion of losses to production losses and was very sensitive to the estimate of mortality rate (Velthuis et al., 2010). However, there is no accurate source in this study for the estimation of these indices. In a recent study,

Figure 3. Increase in the percentage of involuntary culling (IC; % of the total number of cows in the herd) for the period from outbreak onset until February 2007. Separate graphs are presented for herds affected in September, October, and November. Whiskers represent 95% confidence intervals.

economic losses caused by reduced milk and increased mortality were analyzed for the Netherlands. The authors calculated a loss of €48/milking cow because of milk loss and a 3.2-fold increase in the incidence of mortality in affected herds (van Schaik et al., 2008). That analysis was based on a comparison of affected and control herds. The authors did not attempt to correlate economic losses with extent of exposure to the pathogen or time of infection. The methodology used to calculate milk loss was based on a comparison of milk production in affected and nonaffected herds during the outbreak period. The main shortcoming of this approach is that there is a significant difference in milk production between herds, regardless of the studied infection. This might significantly confound the estimation of losses. Indeed, in the current study, analysis of milk production outside of the outbreak period, during periods in which no other infections were abundant, showed significant differences in milk production between the affected and nonaffected herds. Our analysis

Figure 4. Number of corpses disposed of at the Israeli Central Facility for Corpse Disposal (Ein-Hamifratz, Israel) during the epizootic hemorrhagic disease virus outbreak period.

methods enabled us to control for herd effect on milk production and hence provided an estimate of net loss because of the outbreak itself, after adjusting for this potential confounder. Other potential sources of bias in such an analysis relate to monthly and yearly changes in milk production within herds. These confounders were dealt with by including data from years before and after the outbreak to account for a possible yearly trend in milk production. The specific effect of month and year was controlled for by their inclusion in the model. This analysis enabled us to specify the approximate timing of the losses and to correlate them with disease onset, which is highly important because of the disease's short duration.

The SDE estimation from the ICFCD registry was 31% lower than the estimation from our analysis. This difference can be explained by underreporting or underdiagnosis of EHDV cases; we analyzed increased mortality for any reason, whereas in the ICFCD registry, only EHDV-presumed diagnoses are reported. Therefore, the overall similarity between the 2 data sources further supports the validity of the results generated from this study.

Figure 5. Milk loss per milking cow for the outbreak period in 4 categories of epizootic hemorrhagic disease virus seroprevalence. Black bars = cooperative farms; grey bars = family farms. Whiskers represent 95% confidence intervals.

Our aim in this study was to estimate the immediate production losses caused by reduction in milk production and increase in mortality. However, other factors influencing production, such as increased SCC, a higher rate of abortions, decreased reproductive efficiency, increased periparturient morbidity, and increased veterinary costs should also be considered as economic factors in dairy cattle diseases (Ott et al., 2003; Yeruham et al., 2003). Our analysis revealed no significant changes in SCC, fat, or protein percentage in the milk from the affected herds (data not shown). Increases in abortions and decreases in reproductive efficiency are difficult to estimate in such acute diseases because there are many other causes for these events and the timing of the infection effect cannot be readily predicted. Our overall impression and crude analysis of these variables in affected versus nonaffected herds showed no significant differences (data not shown). We therefore did not include them in our calculation of production losses.

The advantage of using a statistical method such as kriging for interpolation is that variance can be calculated for the estimates. By incorporating this variance into the simulations, we could calculate the uncertainty

Table 2. Estimated milk loss and increase in involuntary culling (average and 95% confidence interval) on cooperative and family farms during the epizootic hemorrhagic disease virus (EHDV) outbreak in 2006

EHDV seroprevalence (%)	Farm type ¹	Estimated cows on affected farms (n)	Milk decrease/cow (kg)	Total milk loss (1,000 kg)	Increased involuntary culling (% of herd)	Total increase in involuntary culling (n of cows)
75–100	C	9,447 (7,005 to 11,890)	205 (133 to 277)	1,937 (1,081 to 2,793)	1.42 (0.91 to 1.93) ²	134 (73 to 195)
	F	4,126 (1,641 to 6,611)	133 (–58 to 324)	549 (–350 to 1,448)		59 (18 to 100)
50–75	C	7,380 (4,388 to 10,372)	169 (22 to 315)	1,247 (82 to 2,412)	0	105 (48 to 162)
	F	5,665 (2,742 to 8,588)	113 (–78 to 305)	640 (–544 to 1,824)		80 (29 to 131)
25–50	C	9,126 (5,851 to 12,401)	90 (18 to 163)	821 (104 to 1,538)	0	0
	F	6,960 (1,777 to 3,478)	20 (–161 to 264)	139 (–1,068 to 1,346)		0
Total		42,704 (35,504 to 49,904)		5,333 (2,977 to 7,689)		378 (250 to 506)

¹C = cooperative farm; F = family farm.

²Value is the same for rows 1–4 because it is calculated for the first 4 categories combined.

Figure 6. Increase in percentage of involuntary culling during the outbreak period in herds belonging to 4 categories of epizootic hemorrhagic disease virus seroprevalence. Whiskers represent 95% confidence intervals.

of the total loss estimates. The wide confidence intervals of the calculated estimates result from the high variance of milk production and mortality within and between the herds. The small sample size used for estimating seroprevalence also affected accuracy and caused an increase in uncertainty. A possible weakness of the current study is the overrepresentation of cooperative herds in the study sample. However, comparison of indices like milk production, total cull, and SCC as well as seroprevalence of EHDV showed no statistically significant difference between the affected herds included in the study and the ones that were not included. Nevertheless, type of herds was included in the analysis to control for possible differences between the family and cooperative herds. Interpolation of milk loss was performed separately for each type of herd. There was a high uncertainty as to the estimation of reduction in milk production in the family herds because of their small number in the study. Therefore results for these herds were statistically insignificant though they showed the same association between EHDV seroprevalence and milk loss as was observed in cooperative herds.

CONCLUSIONS

This study demonstrates the significance of production losses associated with outbreak of EHDV. We believe that because of the similarity of clinical signs between EHDV and BTV-8, this study's results can be used for estimation of milk losses and mortality in dairy cattle caused by BTV-8 or other cattle-virulent BTV. This can be performed after taking into account the differences in the value of milk loss and mortality between Israel and other countries. Because there is no available vaccine for EHDV and there are many doubts as to the effectiveness of animal movement restrictions

Figure 7. Kriging-interpolated epizootic hemorrhagic disease virus seroprevalence for Israel. White dots represent the dairy farms in Israel. Color version available in online PDF.

on virus spread, the cost of prevention measures cannot be estimated currently. However, estimation of production losses shows that there is high economic worth in using an effective vaccine to prevent such an outbreak in regions prone to such outbreaks.

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