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Original article

Reduction in milk yield associated with *Mycobacterium avium* subspecies *paratuberculosis* (*Map*) infection in dairy cows

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Abstract – To assess the profitability of control schemes for *Mycobacterium avium* subspecies *paratuberculosis* (*Map*)-infection implemented in dairy herds, accurate estimates of its production effects are needed. This study aimed at quantifying the variation in milk yield of dairy cows according to their *Map*-infection status. The cow-status was determined by combining (i) its testing(s)-result(s) (serum ELISA, faecal culture (FC), PCR, Ziehl staining), (ii) the *Map*-status of its herd, and (iii) its possible vaccination against *Map*. A total of 15 490 cows in 569 herds located in western France was considered. The effect on test-day milk yield (TDMY) of the cow-status to *Map* was assessed separately in parity 1, 2 and 3 or more, using mixed linear models, after adjustment for herd-season (random), days in milk and breed. Average TDMY was significantly lower in cows from herds with at least one *Map*-infected cow (defined as positive herds). Individual TDMY showed a reduction ranging from 1.58 to 3.30, 2.03 to 2.51, 5.36 to 7.20 kg/day ($P < 0.001$) depending on parity for unvaccinated cows and testing ELISA-positive, PCR- or FC-positive, and Ziehl-positive, respectively, compared to cows in *Map*-free herds. The loss in milk yield increased with increased parity in ELISA-positive and Ziehl-positive cows. Cows that were both tested ELISA-positive and vaccinated had a smaller loss in TDMY than those that were unvaccinated. The estimates from this study can be used to further assess the economic impact associated with *Map*-infection in dairy herds or to help in the culling decisions regarding infected cows.

dairy cow / milk yield / *Mycobacterium avium* subsp. *paratuberculosis*

1. INTRODUCTION

Paratuberculosis is a chronic infectious disease of domestic and wild ruminants, caused by *Mycobacterium avium* subspecies *paratuberculosis* (*Map*). Diseased animals contract diarrhoea, associated with progressive weight loss and death [1]. Paratuberculosis is world-wide distributed [7], and highly prevalent in some areas. Approximately 50% of investigated dairy herds have been reported to be infected in Denmark[1], The Netherlands [11], Michigan state [6] and Canada [17]. In addition to animal health concerns, it has been suggested that *Map* could be involved in Crohn's disease in

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[1] Nielsen S.S., Agger J.F., Prevalence of paratuberculosis in Danish dairy herds, in: Salman M.D., Morley P.S., Ruch-Gallie R. (Eds.), Proc. 9th ISVEE symposium, Breckenridge, Colorado, 2000, pp. 267–269.

humans [2], although this hypothesis is currently highly debated.

In that context, different voluntary control programmes have been implemented in a number of countries [7], but with varying success. Because no effective treatment against paratuberculosis exists, available control schemes are mainly based on protection of susceptible animals through improved management practices and removal of animals found to be infected after testing (test-and-cull strategy). Such control schemes are labour-intensive and often expensive (in terms of testing and replacement heifers). The cost/benefit ratio of some strategies (especially those based on a high culling of positive-tested animals), when weighed against the economic losses associated with *Map*-infection, is currently challenged[2].

Thus, a sound ex-ante assessment concerning the profitability of alternative control schemes for *Map*-infection that could be implemented on farms is still very much needed. It requires, in a preliminary step, to get accurate estimates of production effects – milk yield, reproductive performance, longevity – associated with *Map*-infection.

Estimates of reduced milk yield associated with *Map*-infection are abundant [3,4, 8–10, 15–17, 19]. Nevertheless, they were only assessed by comparing milk yield for those positive-tested versus negative-tested cows both of which come from infected herds, i.e. comprised of at least one infected cow. Because of the long incubation period of *Map*-infection and of the poor sensitivity of diagnostic tests [13] leading to the existence of false-negative animals in infected herds, our hypothesis is that estimates found in the literature might be underestimated.

This study was aimed at quantifying the variation in individual test-day milk yield (TDMY) of dairy cows according to their *Map*-infection status in French farming conditions, by taking as a reference cows from herds certified to be free of *Map*-infection.

2. MATERIALS AND METHODS

2.1. Herds, animals and records

Data came from herds located in Morbihan (western France) that were monitored for *Map*-infection and enrolled in the official Milk Recording scheme. For each herd, information on individual tests for *Map*-infection (including test date(s)) and test day milk yield of lactating cows between 1st January 1998 and 31st December 2002 were available.

The tests used to detect *Map*-infection were ELISA (Pourquier® ELISA paratuberculose serum, Institut Pourquier, France), PCR on serum (Adiavet® PARATUB, Adiagène, France), faecal culture and Ziehl-Neelsen faecal staining, which were selected considering both the epidemiological and clinical context of the herd.

The *Map*-infection control scheme includes tests (implemented usually two-years apart) for all adult cows (at any stage of lactation) which are present within the concerned herd on the testing date. Due to early culling, especially that of positive-tested cows, most cows are tested only once (e.g. 79.6% in the present dataset), using mainly serological or faecal culture techniques (in 82.9 and 15.7% of cases respectively). The proportions of cows tested twice and three times or more are here 19.5 and 1.9% respectively. Cows tested twice or more are either repeatedly tested using

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[2] Kudahl A., Ostergaard S., Sørensen J.T., Nielsen S.S., A stochastic model simulating paratuberculosis in a dairy herd, in: Kudahl A., Economic consequences of paratuberculosis control in dairy cattle herds, Ph.D. dissertation, Foulum, 2004, pp. 47–80.

the same technique, or mainly ELISA-tested at first then faecal culture or PCR-tested to ascertain their infection status. The Ziehl-Neelsen faecal staining is only performed on cows showing clinical signs attributable to paratuberculosis.

2.2. *Map*-infection cow status

Each cow was assigned a *Map*-infection status, defined by taking into account not only the results of its individual testing(s), but also the status of its herd, and its possible vaccination.

Most cows being tested once, the individual status was not considered as a time-dependent covariate. From results of individual testings, and by accounting for the flow of test strategies, a cow was considered negative (i.e. not testing positive for any of the technique(s)); ELISA-positive; FC-positive; PCR-positive and Ziehl-positive, according to the principles displayed in Table I. For instance, a cow was considered FC-positive, if it was positive-tested based on faecal culture, negative-tested based on PCR and Ziehl (if implemented), and regardless of the serological response provided by an ELISA-test (if implemented).

Three herd statuses of *Map*-infection were defined: Certified-free, Negative, and Positive. In herds certified to be free of *Map*-infection, named hereafter "Certified-free herds", (i) all animals present over 24 months were tested using ELISA and found to be negative, (ii) no animal showed clinical signs of paratuberculosis (certified by both the farmer and the veterinary practitioner) in the past three years, and (iii) every newly-introduced animal was serologically-tested. A Negative herd was defined as one in which all tested cows were found to be negative. In these herds, not all adult cows were necessarily tested, whereas the testing was exhaustive in Certified-free herds. However, given the lack of sensitivity of individual tests, the Negative herds with less than 12 individuals tested were excluded, to limit the likelihood of false-negative status at herd level. Lastly, a herd was considered Positive if at least one cow was positive-tested. Thus, using this information, possible differences in milk yield between cows in a Negative herd and cows qualified negative in a Positive herd could be assessed. Information on vaccination against *Map*-infection when tested was also taken into account. A total of 14 *Map*-infection cow statuses was finally considered (Tab. II).

2.3. Modelling

The effect on TDMY of the *Map*-infection cow status was assessed using a mixed linear model, after adjustment for herd-season (random), breed, and days in milk on test day. Because (i) lactation curves in primiparous, second lactation and older cows have different shapes, and (ii) the *Map*-infection is expected to progress with the aging-process and production losses are expected to increase with parity, the model was run separately for cows in parity 1, parity 2, and parity 3 and more (parity was included as a confounder for the latter group), similarly to [8].

Preliminary investigations on the variation in milk yield associated with a possible previous occurrence of vaccination against *Map* showed that milk yield of vaccinated and unvaccinated cows differed significantly ($P < 0.05$) only in ELISA positive-tested cows. Therefore, owing to the distribution of cows according to their *Map*-infection status (Tab. II), cows with the same individual and herd statuses were gathered irrespectively of their status of vaccination, except those that were ELISA positive-tested. Indeed, vaccination influences responses to serological tests [12], and cows that are both ELISA

Table I. Definition of individual statuses from combined responses of individual tests.

Individual status	Individual test			
	ELISA	Faecal culture	PCR	Ziehl staining
Negative	–/NT[a]	–/NT	–/NT	–/NT
ELISA-positive	+	–/NT	–/NT	–/NT
FC-positive	–/+/NT[b]	+	–/NT	–/NT
PCR-positive	–/+/NT	–/+/NT	+	–/NT
Ziehl-positive	–/+/NT	–/+/NT	–/+/NT	+

[a] Negative-tested or untested.

[b] Negative-tested or positive-tested or untested.

Table II. Definition and distribution of *Map*-infection cow statuses (n = 15 490).

MAP status[a]	Individual status	Herd status	Vaccination	%	Milk yield (kg/d)	
					Mean[b]	std
I–/H–/V–	Negative	Negative	No	23.83	26.5	8.1
I–/H–/V+	Negative	Negative	Yes	0.56	25.6	7.8
I–/FH/V–	Negative	Certified free	No	7.35	27.5	8.1
I–/FH/V+	Negative	Certified free	Yes	0.03	28.2	7.1
I–/H+/V-	Negative	Positive	No	55.09	25.9	8.3
I–/H+/V+	Negative	Positive	Yes	7.15	25.5	8.0
E+/H+/V–	ELISA +	Positive	No	1.49	23.7	8.1
E+/H+/V+	ELISA +	Positive	Yes	2.09	25.7	8.2
C+/H+/V–	Faecal culture +	Positive	No	0.92	25.3	8.3
C+/H+/V+	Faecal culture +	Positive	Yes	0.05	23.5	7.0
PCR+/H+/V–	PCR +	Positive	No	0.03	26.6	8.8
PCR+/H+/V+	PCR +	Positive	Yes	0.01	20.6	8.5
Z+/H+/V–	Ziehl +	Positive	No	1.16	21.4	8.4
Z+/H+/V+	Ziehl +	Positive	Yes	0.25	24.0	9.7

[a] I–: Individual status "Negative"; E+: individual status "ELISA+"; C+: individual status "Faecal culture +"; PCR+: individual status "PCR +"; Z+: individual status "Ziehl+"; H–: herd status "Negative"; FH: herd status "certified- free"; H+: herd status "Positive"; V–: "Unvaccinated"; V+: "Vaccinated".

[b] Crude milk yield on test day.

positive-tested and vaccinated are possibly non-infected. In addition, FC-positive and PCR-positive cows were gathered into a group including presumed preclinical shedders. Finally, owing to the poor sensitivity of diagnostic tests, the probability for a cow to be truly-infected while testing negative once (false-negative) is higher than that of a cow tested twice or more. In this context, if *Map*-infection is associated with a decrease in milk yield, our hypothesis was that milk yield in the former case was lower than in the latter. Thus, the cows testing negative once were distinguished

Table III. Average milk yield, adjusted reduction in test-day milk yield (and 95% confidence interval) according to *Map*-infection cow status (122680 test-days from 15490 cows in 569 dairy herds).

Map-infection Cow-status[a]	Parity					
	1		2		⩾ 3	
	avMY[b]	Loss (95CI)[c]	avMY	Loss (95CI)	avMY	Loss (95CI)
I–/H– tested once	23.8	1.14 (0.49–1.79)	27.4	0.21 (–0.65–1.06)	26.5	0.9 (–0.02–1.82)
I–/H– tested twice or more	24.9	0.15 (–0.75–2.25)	24.0	1.04 (–0.25-2.33)	28.8	0.35 (–0.46–1.16)
I–/FH	24.7	0	28.1	0	29.3	0
I–/H+ tested once	22.6	1.27 (0.65–1.88)	25.7	1.21 (0.42–2.00)	26.5	2.08 (1.34–2.83)
I–/H+ tested twice or more	22.6	0.34 (–0.33–1.02)	26.4	0.29 (–0.55–1.13)	27.2	1.62 (0.87–2.38)
E+/H+/V–	21.6	1.58 (0.82–2.34)	22.8	2.20 (1.22–3.19)	24.2	3.30 (2.54–4.06)
E+/H+/V+	23.0	0.82 (0.13–1.51)	25.6	1.25 (0.30–2.20)	28.0	1.46 (0.77–2.14)
SH+/H+	20.7	2.51 (1.55–3.47)	25.5	2.03 (0.94–3.12)	26.6	2.29 (1.33–3.25)
Z+/H+	17.6	5.36 (4.42–6.29)	21.3	6.23 (5.20–7.25)	23.8	7.20 (6.27–8.13)

[a] I–: Individual status “negative”; E+: individual status “ELISA-positive”; SH+: individual status “preclinical shedders”; Z+: individual status “Ziehl-positive”; H-: herd status “negative”; FH: herd status “certified-free”; H+: herd status “positive”; V–: “Unvaccinated”; V+: “Vaccinated”.

[b] Average milk yield (in kg/d) on test day.

[c] Adjusted reduction in milk yield (in kg/d) in deviation from I-/FH cows (with 95% Confidence Interval).

from those testing negative twice or more. The *Map*-infection cow status was then distributed over 9 classes (Tab. III).

The general mixed model (MIXED procedure)[3,4] was written as follows:

$$Y_{ijklm} = m + STATUS_i + DIM_j + B_l + H_m + e_{ijklm} \quad (1)$$

where Y is the milk yield on each test day, m is the overall mean, $STATUS_i$ is the fixed effect of status i of the *Map*-infection (9 classes), DIM_j is the fixed effect of class j of days in milk (15 classes), B_l is the fixed effect of class l of breed (2 classes), H_m is the effect of herd-season m (random effect, 1 632 classes; 3 seasons (April to July, August to October, November to March) being considered in each studied herd), and e_{ijklm} is the residual. The median number of test days per cow within a lactation being of 8 (range: 1 to 14), a standard Variance Component structure was used, to account for correlation among test days. The model was run considering, for a given cow, test days in the lactation concomitant to the testing used to define its *Map*-infection status. The cow taken as a reference was a cow in Certified-free herds.

3. RESULTS

3.1. Descriptive results

A total of 122 680 test days (34 934; 29 716 and 58 030 in primiparous, parity 2 and parity 3 and more respectively), taken from 15 490 cows located in 569 herds was considered for analysis. Distribution of cows according to their *Map*-infection status and descriptive statistics for crude milk yield on test days in the concomitant lactation are shown in Table II.

3.2. Impact of *Map*-infection cow status on milk yield

Whatever the parity-group concerned, *Map* status was significantly ($P < 0.05$) associated with milk yield on test day (Tab. III).

TDMY was significantly lower in positive-tested cows. Individual TDMY showed a reduction ranging, depending on parity, from 1.58 to 3.30, 2.03 to 2.51, 5.36 to 7.20 kg/day ($P < 0.001$) for cows which were unvaccinated and testing ELISA-positive, PCR- or FC-positive, and Ziehl-positive, respectively, compared to cows in Certified-free herds. In addition, the loss in milk yield increased with increased parity in ELISA-positive and Ziehl-positive cows (Tab. III).

Cows which were found negative in Positive herds (i.e. herds with at least one *Map*-infected cow) after having been tested twice or more, did not experience any significant loss in milk yield (except cows in parity 3 or more), whereas all those tested only once had a significant ($P < 0.05$) decrease in milk yield ranging from 1.21 to 2.08 kg/d depending on parity. ELISA-tested positive and vaccinated (E+/H+/V+) cows had a smaller loss in milk yield than those unvaccinated (E+/H+/V–).

Cows in a Negative herd (I–/H) did not experience any significant loss in milk yield, compared to cows in a Certified-free herd (I-/FH), except the primiparous cows tested only once.

Adjustment variables were significantly ($P < 0.001$) associated with test day milk yield (Tab. IV). Variations in milk yield depending on days in milk demonstrated the classical shape of the lactation curve.

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[3] Littel R.C., Milliken G.A., Stroup W.W., Wolfinger R.D., SAS System for Mixed Models, SAS Institute Inc., Cary, NC, 1996.

[4] SAS Institute Inc., SAS/STAT User's guide, changes and enhancements through release 6.11. SAS Institute Inc., Cary, NC, 1996.

Table IV. Effect of adjustment variables on test-day milk yield (122 680 test-days from 15 490 cows in 569 dairy herds).

Variable and category	Parity					
	1		2		⩾3	
	avMY[a]	Δ MY (95CI)[b]	avMY	Δ MY (95CI)	avMY	Δ MY (95CI)
Days in milk						
0–14	25.5	–1.57 (–.3.63;0.49)	30.0	–5.15 (–7.94;–2.36)	29.7	–6.28 (–8.91;–3.65)
15–29	27.4	–0.87 (–1.93;0.19)	33.5	–1.36 (–3.11;0.38)	32.8	–2.53 (–3.94;–1.13)
30–44	27.3	0	34.0	0	35.9	0
45–59	27.1	–0.18 (–0.56;0.20)	33.4	–0.79 (–1.29;–0.29)	35.8	–0.40 (–0.79;–0.01)
60–74	26.4	–0.81 (–1.19;–0.44)	32.1	–1.94 (–2.44;–1.44)	34.4	–0.20 (–0.58;0.19)
75–89	25.7	–1.39 (–1.77;–1.02)	30.7	–3.24 (–3.73;–2.75)	33.1	–2.81 (–3.20;–2.43)
90–119	25.1	–2.06 (–2.41;–1.72)	29.4	–4.62 (–5.06;–4.17)	31.2	–4.80 (–5.15;–4.45)
120–149	24.2	–3.01 (–5.31;–0.70)	27.9	–6.13 (–6.58;–5.68)	29.3	–6.74 (–7.09;–6.40)
150–179	23.4	–3.82 (–4.16;–3.47)	26.6	–7.55 (–8.00;–7.10)	27.4	–8.55 (–8.90;–8.20)
180–209	22.7	–4.50 (–4.85;–4.15)	25.0	–9.01 (–9.46;–8.55)	25.8	–10.11 (–10.47;–9.76)
210–239	21.9	–5.16 (–5.51;–4.81)	23.6	–10.12 (–10.58;–9.66)	24.4	–11.46 (–11.81;–11.10)
240–269	21.1	–5.96 (–6.32;–5.61)	22.1	–11.69 (–12.15;–11.23)	22.7	–13.21(–13.57;–12.85)
270–299	20.1	–6.77 (–7.13;–6.41)	21.1	–12.69 (–13.15;–12.22)	21.0	–14.85(–15.21;–14.48)
300–329	20.5	–6.38 (–6.75;–6.02)	21.1	–12.63 (–13.11;–12.15)	21.3	–14.48 (–14.86;–14.11)
330–359	21.0	–6.08 (–6.45;–5.71)	21.7	–11.15 (–11.65;–10.65)	21.7	–13.07 (–13.46;–12.69)
⩾ 360	20.9	–5.90 (–6.28;–5.52)	21.7	–11.13 (–11.64;–10.63)	21.9	–12.84 (–13.24;–12.44)
Breed						
Holstein	23.6	0	26.8	0	27.7	0
Other	17.5	–5.46 (–5.78;–5.14)	19.9	–5.97 (–6.44;–5.50)	20.7	–6.91 (–7.27;–6.55)

[a] Average milk yield (crude data in kg/d).

[b] Adjusted variation in test day milk yield (in kg/d) (95% confidence interval).

4. DISCUSSION

Milk yield was found to be significantly lower in cows with positive tests for *Map*-infection. As expected, the largest loss (5.4 to 7.2 kg/d) was reported in Ziehl positive-tested cows; this type of testing was implemented in animals suspected to experience clinical paratuberculosis. Presumed preclinical shedders (i.e. FC or PCR positive-tested), as well as unvaccinated and ELISA-positive cows had a lower reduction in milk yield (of about 2 kg/d), suggesting that the reduction in milk yield starts early in a cow's productive career, before clinical signs might have occurred [5].

Our estimates have to be cautiously compared to those reported in the literature, mainly because cows taken as a reference were here negative-tested in Certified-free herds, whereas previous studies provided estimates related to milk yield in negative-tested cows from infected herds. A decrease after 100 DIM by 205 kg [19] and in 305-day milk yield by 548 and 1485 kg (in [3] and [16] respectively) was reported in faecal culture-positive tested cows, whereas in this study it was by about 2 kg/d. The estimate associated with being ELISA-positive found in the present study (1.5 to 3.3 kg/d) appeared to be equivalent to or slightly higher than most previous findings reporting a significant decrease varying from 375 to 575 kg (in 305-day milk yield[5] [3, 9, 15, 16]), and by about 3 kg/d per 1 standardized-Optical-Density unit increase – with most positive-tested cows showing a standardized Optical-Density below 0.70 in this study [8]. Thus, our hypothesis stating that estimates reported in the literature could be underestimated was here confirmed.

Significantly lower milk yield was also observed in once-tested negative cows from herds containing at least one positive-tested animal (Positive herd). This finding could be partly explained by the lack of sensitivity of the tests applied at the individual level [13], leading to the existence of false-negative animals in this group. This assumption was supported by the fact that, in these herds, cows (except those in parity 3 or more) with more than one negative test did not show any significant loss in milk yield.

Compared to cows in Certified-free herds, cows from Negative herds showed a significant reduction in milk yield, only when they were primiparous. The magnitude of loss observed in these cows (about 1 kg/d) was similar to that found in negative-tested primiparous cows located in Positive herds. Based on this observation, a possible misclassification of some so-called Negative herds cannot be excluded. This assumption is supported by the fact that not all cows were tested in the negative herds, which could have led to consider herds negative, which would have been considered positive in the case of exhaustive testing (however, in the present study, herds classified negative based on less than 12 cows being tested were excluded). In addition, only primiparous cows had a significantly lower milk yield, which was found almost equivalent to that of seropositive ones (Tab. III). It is then very likely that some truly infected primiparous cows were here falsely considered negative, owing to the low sensitivity of ELISA tests when applied to primiparous cows, in comparison to multiparous ones [14]. However, it cannot be excluded that the extra reduction in milk yield in primiparous cows may be partly related to differences in herd management and genetic makeup between Negative and

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[5] Goodell G.M., Hirst H., Garry F., Dinsmore P., Comparison of cull rates and milk production of clinically normal dairy cows grouped by ELISA *Mycobacterium avium paratuberculosis* serum antibody results, in: Salman M.D., Morley P.S., Ruch-Gallie R. (Eds.), Proc. 9th ISVEE symposium, Breckenridge, Colorado, 2000, pp. 897–899.

Certified-free herds. This possible confounding bias was here limited by accounting for a random herd effect in models.

On the contrary to [8] who reported the highest milk losses in parities 1 and 2, and only in three or more parity for cows with very high antibody levels, the reduction in milk yield in positive-tested cows was here found to increase with increasing parity, in agreement with the assumption that production losses increased with the infection stage (aging process).

Cows which were both ELISA-tested positive and vaccinated had a smaller loss in TDMY than those unvaccinated. A possible explanation could be a lower decrease in milk yield in relation to a lower severity of cases in vaccinated cows [18]. However, the fact that milk yield for vaccinated and unvaccinated cows differed significantly ($P < 0.05$) only in ELISA positive-tested cows did not support this hypothesis. In relation to the interference of vaccination on immune responses [12], it is more likely that truly infected and truly non-infected animals (i.e. false-positive) coexisted among the cows that were both ELISA tested-positive and vaccinated, leading to a mean reduction in milk yield to a lesser degree in that group.

Because the present study investigated *Map*-infection cow statuses compared to cows in Certified-free herds, the provided estimates might be deemed more reliable to assess the economic impact of *Map*-infection. Furthermore, on the contrary to previous studies, a larger number of statuses were here jointly studied, based not only on responses obtained from detection methods currently performed at the individual level, but also on both the epidemiological environment of the animal (herd status) and the existence of a possible vaccination. This strategy allowed us to confirm our hypotheses about existing variations in milk yield between (i) negative and positive-tested cows within a herd; and (ii) vaccinated and unvaccinated ELISA positive-tested cows. It also provided a comprehensive assessment for most cow statuses of *Map*-infection which can be encountered in dairy herds.

This study demonstrates that *Map*-infection may have a large economic impact on milk yield in dairy herds, which could occur in the absence of any clinical sign attributable to paratuberculosis. The estimates provided can be used to further assess the profitability of control plans for *Map*-infection in dairy herds and to help in the culling decisions regarding infected cows.

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REFERENCES

[1] Chiodini R.J., van Kruiningen H.J., Merkal R.S., Ruminant paratuberculosis (Johne's disease): the current status and future prospects, Cornell Vet. (1984) 74:218–262.

[2] Chiodini R.J., Rossiter C.A., Paratuberculosis: a potential zoonosis? Vet. Clin. North Am. Food Anim. Pract. (1996) 12:457–467.

[3] Hendrick S.H., Kelton D.F., Leslie K.E., Lissemore K.D., Archambault M., Duffield T.E., Effect of paratuberculosis on culling, milk production, and milk quality in dairy herds, J. Am. Vet. Med. Assoc. (2005) 227:1302–1308.

[4] Johnson Y.J., Kaneene J.B., Gardiner J.C., Lloyd J.W., Sprecher D.J., Coe P.H., The effect of subclinical *Mycobacterium paratuberculosis* infection on milk production in Michigan dairy cows, J. Dairy Sci. (2001) 84:2188–2194.

[5] Johnson-Ifearulundu Y.J., Kaneene J.B., Epidemiology and economic impact of subclinical Johne's disease: a review, Vet. Bull. (1997) 67:437–447.

[6] Johnson-Ifearulundu Y.J., Kaneene J.B., Distribution and environmental risk factors for paratuberculosis in dairy herds in Michigan, Am. J. Vet. Res. (1999) 60:589–596.

[7] Kennedy D., Holmstrom A., Plym Forshell K., Vindel E., Suarez Fernandez G., On-farm management of paratuberculosis (Johne's disease) in dairy herds, IDF Bull. (2001) 362:18–31.

[8] Kudahl A., Nielsen S.S., Sørensen J.T., Relationship between antibodies against *Mycobacterium avium* subspecies *paratuberculosis* in milk and shape of lactation curves, Prev. Vet. Med. (2004) 62:119–134.

[9] Lombard J.E., Garry F.B., MacCluskey B.J., Wagner B.A., Risk of removal and effects on milk production associated with paratuberculosis status in dairy cows, J. Am. Vet. Med. Assoc. (2005) 227:1975–1981.

[10] McNab W.B., Meek A.H., Martin S.W., Duncan J.R., Associations between dairy production indices and lipoarabinomannan enzyme-immunoassay results for paratuberculosis, Can. J. Vet. Res. (1991) 55:356–361.

[11] Muskens J., Barkema H.W., Russchen E., van Maanen K., Schukken Y.H., Bakker D., Prevalence and regional distribution of paratuberculosis in dairy herds in the Netherlands, Vet. Microbiol. (2000) 77:253–261.

[12] Muskens J., van Zijderveld F., Eger A., Bakker D., Evaluation of the long-term immune response in cattle after vaccination against paratuberculosis in two Dutch dairy herds, Vet. Microbiol. (2002) 86:269–278.

[13] Nielsen S.S., Nielsen K.K., Huda A., Condron R., Collins M.T., Diagnostic techniques for paratuberculosis, IDF Bull. (2001) 362:5–17.

[14] Nielsen S.S., Enevoldsen C., Grohn Y.T., The *Mycobacterium avium* subsp. *paratuberculosis* response by parity and stage of lactation, Prev. Vet. Med. (2002) 54:1–10.

[15] Nordlund K.V., Goodger W.J., Pelletier J., Collins M.T., Associations between subclinical paratuberculosis and milk production milk components and somatic cell counts in dairy herds, J. Am. Vet. Med. Assoc. (1996) 208:1872–1876.

[16] Spangler E., Bech-Nielsen S., Heider L.E., Diagnostic performance of two serologic tests and fecal culture for subclinical paratuberculosis, and associations with production, Prev. Vet. Med. (1992) 13:185–195.

[17] Van Leeuwen J.A., Keefe G.P., Tiwari A., Seroprevalence and productivity effects of infection with bovine leukemia virus, *Mycobacterium avium* subspecies *paratuberculosis*, and *Neospora caninum* in Maritime Canadian dairy cattle, Bovine Pract. (2002) 36:86–91.

[18] Wenting G.H., Bongers J.H., Zeeuwen A.A., Jaartsveld F.H., Incidence of paratuberculosis after vaccination against *M. paratuberculosis* in two infected dairy herds, Zentralbl. Veterinarmed. B (1994) 41:517–522.

[19] Wilson D.J., Rossiter C., Han H.R., Sears P.M., Association of *Mycobacterium paratuberculosis* infection with reduced mastitis, but with decreased milk production and increased cull rate in clinically normal dairy cows, Am. J. Vet. Res. (1993) 54:1851–1857.