Economic impact of paratuberculosis in dairy cattle herds: a review

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ABSTRACT: Paratuberculosis (PTB) is a disease which causes considerable economic losses to producers of livestock, particularly dairy cows. Nowadays PTB is one of the most prevailing and costly infectious diseases of dairy cattle. The purpose of the present study was to review economic losses, which may be caused by *Mycobacterium avium* subsp. *paratuberculosis* (*MAP*) above all in herds of dairy cattle. The most important losses caused by the presence of clinically ill animals have been thoroughly described: loss of milk production and poor body condition followed by death or culling. In contrast, losses arising from a subclinical disease have not been well documented and contradictory results have been published to date. The calculation of losses caused by PTB depends to a certain degree on the production system in a herd, efficiency level, herd management system and other factors. Direct economic losses are above all caused by decreased milk production concurrent to increased incidence of mastitis, changes in milk parameters and increased somatic cell counts, reproductive dysfunctions, poor feed conversion, shortened production age and increased predisposition to other diseases etc. Indirect economic losses are caused by premature culling of animals and their unrealized future income, expenses for non-active production, herd replacement, diagnostic testing, "unnecessary" veterinary care and establishing disease control programmes. Genetic value of animals and their progeny is lost. Last but not least, the reputation of the farm where *MAP* infected animals are kept is lost for a long-time, which is also important.

Keywords: Johne's disease; *MAP*; dairy cattle; economic losses; Crohn's disease; IS*900*

List of abbreviations: **AGIDT** = agar gel immunodiffusion test; **BVD** = bovine viral diarrhoea; **CFT** = complement fixation test; **EBL** = enzootic bovine leucosis; **ELISA** = enzyme-linked immunosorbent assay; **GBP** = Greit Britain Pound; **IBR** = infection bovine rhinotracheitis; **LA%** = lactation percentage; **LAM** = Lipoarabinomannan; ***MAP*** = *Mycobacterium avium* subsp. *paratuberculosis*; **ME** = mature equivalent; **NEB** = negative energy balance; **NOK** = Norwegian Crown; **PTB** = paratuberculosis; **SCC** = somatic cell count; **USD** = United States Dollars; **USDA** = United States Department of Agriculture

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1. Introduction

Paratuberculosis (PTB, Johne's disease) is nowadays viewed as one of the most serious and widespread chronic bacterial diseases of ruminants in agriculturally developed countries (Ayele et al., 2001; Kennedy and Benedictus, 2001; Vecerek et al., 2003; Hruska, 2004). The etiologic agent of PTB, *Mycobacterium avium* subsp. *paratuberculosis* (*MAP*) is a slowly growing, mycobactin-dependent acid-fast bacterium containing specific insertion sequence IS*900* (Sweeney, 1996).

Infected cows may have clinical signs such as persistent diarrhoea and progressive weight loss; however, asymptomatic animals may shed *MAP* with colostrum and milk, particularly in later stages of the disease (Sweeney et al., 1992; Streeter et al., 1995). Colostrum and milk fed to calves may be significant sources of *MAP* (Ayele et al., 2001, 2005). Calves younger than six months are most susceptible; most infections are assumed to be acquired during the first 6 months of life (Larsen et al., 1975).

The primary source of *MAP* transmission is faecal contamination of a calf's environment, including contamination of milk and feed, resulting in the ingestion of the agent by the calf (Sweeney, 1996). The calf may also get infected from the mother *in utero*. Such mothers may be asymptomatic (Kopecky et al., 1967; Seitz et al., 1989). The first report of congenital infection was made in 1929 by Alexjeff-Goleff (Alexjeff-Goleff, 1929, as quoted by Kopecky et al., 1967). Less important sources include sperm from infected bulls (Larsen et al., 1981; Ayele et al., 2004) and embryo transfer (Rhode and Shulaw, 1990). Wild ruminants (Pavlik et al., 2000a; Machackova et al., 2004; Machackova-Kopecna et al., 2005) may also be a potential source of *MAP* infection. Due to the fact that *MAP* was also detected in wild animals other than ruminants, e.g.

wild boar (Machackova et al., 2003), wild rabbits (Greig et al., 1999) and invertebrates (Fischer et al., 2001, 2003a,b, 2004a,b, 2005), this risk should also be considered.

MAP is usually introduced to dairy herds through the purchase of infected but clinically normal cattle. Because of the long incubation period, infected heifers, cows or bulls may show no signs of the infection for many years, and will often test negative on serologic and/or faecal culture tests (Sweeney, 1996). All the measures accepted for herd/animal protection from PTB should be based on this knowledge and farmers should not purchase animals infected with *MAP*, particularly from herds with an unknown infection status. In some cattle herds affected with PTB, economic losses may be so high that farming cannot be profitable any more (Benedictus et al., 1987). In contrast Stott et al. (2005) documented that PTB caused less economic losses than other serious diseases.

Economic consequences of PTB have been investigated (Merkal et al., 1975; Buergelt and Duncan, 1978; Abbas et al., 1983; Benedictus et al., 1987; Kormendy et al., 1989; Nordlund et al., 1996; Johnson-Ifearulundu and Kaneene, 1997); particularly in dairy cattle herds from various countries with developed agriculture. However, different criteria, parameters and calculations have been used for the analysis of economic losses. Different authors have used different methods for estimation of economic losses caused by PTB and their findings are difficult to compare. Due to the fact that some of the consequences of this disease cannot be quantified and some of them are only hypothetical, an accurate estimation is impossible.

The purpose of the present study was to review economic losses that may be caused by *MAP*, above all in herds of dairy cattle.

2. Introduction to the economics of animal health

The presence of disease results in lower output (e.g. lower milk yields), than expected and/or in higher levels of input use, e.g. more veterinary inputs (Bennett, 2003). The presence or absence of disease may have an effect not only on production but also on prices (for both outputs and inputs); for example, increased use of veterinary input to control disease may result in increased national output of livestock products, which in turn may result in lower prices for output (Otte and Chilonda, 2000; Bennett, 2003; Losinger, 2005).

Bennett (2003) defined the cost of disease as direct disease cost

$$C = (L + R) + T + P$$

where:

L = defined as the value of the loss in expected output due to the presence of a disease

R = the increase in expenditures on non-veterinary resources due to a disease (farm labour etc.)

T = the cost of inputs used to treat disease

P = the cost of disease prevention measures

The above cited author did not include indirect impact of disease in their model; they only described some of them such as impact on human health, animal welfare, and international trade.

Otte and Chilonda (2000) defined the total cost of disease as a sum of direct and indirect production losses (L) and the control expenditures (E) and they suggest that the cost of a particular disease will vary between production systems. Estimation of expenditures associated with a particular disease represents valuable economic information that provides data for a decision whether to use control measures and assessment of their benefits. The terms 'economic optimum level of the disease and disease control' are used in some studies (McInerney, 1996; Otte and Chilonda, 2000), which are determined by prices of required inputs and products.

3. Economic losses due to paratuberculosis

3.1. Factors affecting the estimation of economic consequences of paratuberculosis

Economic losses caused by PTB vary among regions and farms (Riemann and Abbas, 1983). The reported losses varied with the production and management system, immunological status of the herd and presumably methods of estimation (Kormendy et al., 1989).

Another challenge is the calculation of losses to the dairy industry associated with subclinical *MAP* infection, due to the difficulty in identifying subclinical carriers and assessing the impact of infection on productivity of these animals (Johnson-Ifearulundu and Kaneene, 1997). Adverse impacts

of clinical PTB on milk production, body condition ,and subsequent losses by culling of animals have been well described by Harris and Barletta (2001) and Chaffer et al. (2002). In contrast, specific effects during the subclinical stage of the disease have not been documented as well, and contradictory results have often been obtained. Calculation of losses caused by PTB is associated to a certain degree with the production system of a herd represented by its size, production level, herd management (above all rearing of calves and young animals), and other factors (Dufour et al., 2004).

For example, dairy cattle herds in France are rather small in size (on average 40 cows) in comparison with other countries (Dufour et al., 2004). Due to that fact, the results obtained in one country cannot be directly applied to another one.

3.1.1. Various methods of estimation of economic losses

Determining indirect costs and productivity losses attributable to clinical and subclinical disease is challenging (Jones, 1989). Economic losses attributable to PTB are a result of premature culling, reduced milk production, and loss of body weight in cattle sold for slaughter (Wells and Wagner, 2000). Dufour et al. (2004) classified the losses attributable to PTB into two groups:

(i) Losses caused by the presence of clinically ill animals have been calculated as a sum of the following expenses:

a. The highest amount is the physical loss of a diseased cow and its calf. Farmers' losses are above all caused by the culling of a female calf that is important for future reproduction. Male calves are fattened before they reach slaughter body weight (they are used for the production of veal). Calculation of these losses depends on the number of animals culled from a herd and subsequently replaced.

b. Other financial losses are the costs of veterinary services (treatment of diarrhoea before culling the animals) and for laboratory testing: Ziehl-Neelsen staining, serological and culture examination.

(ii) Losses caused by subclinically infected animals are difficult to estimate in comparison with losses by clinical cases. For instance it is known that, despite the fact that they do not show any clinical sign, the milk production of subclinically infected animals is lower than the production of healthy animals.

Dufour et al. (2004) estimated annual losses in a mean dairy herd in France per one clinical case as 1 940 € and per one subclinical case as 461 €.

3.1.2. Losses caused by paratuberculosis compared with losses caused by other infectious diseases

Chi et al. (2002) determined that in a 50-cow herd, direct production losses and treatment costs due to four infectious diseases: bovine viral diarrhoea (BVD), enzootic bovine leukosis (EBL), PTB and neosporosis. Direct production losses included milk loss, premature culling and reduced slaughter value, mortality loss, abortion and reproductive loss. Treatment costs included veterinary services, medication costs and extra farm labour costs.

The direct production losses to infected herds for BVD, EBL, PTB, and neosporosis were much greater than average total treatment costs. Average herd costs were higher for PTB than the other three diseases despite PTB having the lowest apparent prevalence of infection in a positive herd (7%) because of high premature voluntary culling (20%) and reduced slaughter value (25%) in PTB-infected animals. Total annual costs for an average, infected, 50 cow herds were: USD 2 472 for PTB, USD 2 421 for BVD, USD 2 304 for neosporosis and USD 806 for EBL (Chi et al., 2002).

In contrast Bennett (2003) estimated that annual losses expressed as output loss and input expenditure with treatment and prevention costs caused by PTB are less economically consequential compared to other cattle diseases (e.g. IBR, BVD, mastitis, and lameness). Stott et al. (2005) using a dynamic programme documented that PTB decreases net profit from milk production by about £ 27 per cow and year relative to milk prices. They view these losses as rather low in comparison with other diseases in a dairy farm (such as subclinical mastitis).

3.2. Classification of economic losses

Economic losses may be classified from several aspects (Benedictus et al., 1987; Ott et al., 1999; Otte and Chilonda, 2000; Groenendaal et al., 2002; Bennett, 2003; Groenendaal, 2005). The most commonly used classification is the following:

(i) direct losses

(ii) indirect losses

(i) The following economic losses are classified as direct:

a. The highest losses are caused by mortality of clinically ill animals and by a decreased slaughter value or complete condemnation of slaughtered animals.

b. Decreased milk production from an aspect of quantity and quality, i.e. changes in milk parameters, increased somatic cells counts and increased incidence of mastitis.

c. Due to decreased pregnancy rate and increased post-partum complications, fertility of cows in a herd declines.

d. The feed conversion is poor not only in clinically, but also in subclinically infected animals.

e. Productive age length is decreased in the infected animals.

f. In the *MAP* infected herds, increased predisposition to other chronic diseases (chronic arthritis, rumenitis, dermatitis, mastitis, etc.) was recorded.

(ii) The following economic losses are classified as indirect:

a. Unrealized future income by breeding animals prematurely culled.

b. Increased expenses for idle production.

c. Increased expenses for herd replacement (purchase of young breeding animals).

d. Expenses for diagnostic testing for PTB, or expenses for ineffective veterinary care for clinically ill animals (treatment of chronic diarrhoea, which is usually fatal in high-producing animals or slaughter of such animals) and other veterinary services for animals culled due to infection.

e. Expenses for a control programme.

f. Lost genetic value of highly valuable animals, which are culled from a herd due to suspected infection (such as progeny of infected dams).

g. Expenses associated with trade restrictions imposed by the market or by regulation.

h. Last but not least, the reputation of a farm with *MAP* infected animals is lost for a long-time.

3.3. The true cause of decreased efficiency

Two mechanisms are supposed to be responsible for the decreased efficiency of *MAP* infected animals. One of them is negative energy balance, the other one is impaired cellular immunity (Johnson-Ifearulundu and Kaneene, 1997).

3.3.1. Negative energy balance

Negative energy balance (NEB) is the situation in which intake of feed energy is less than the output of energy from the body (Vandehaar et al., 1995). A higher probability of negative energy balance is assumed in PTB-infected cows because of a decreased nutrient absorption in the intestines. In addition to this malabsorption syndrome, protein losing enteropathy occurs during PTB (Kreeger, 1991). The association between the pathological condition and reduction in feed efficiency, milk production, milk fat and protein production, and slaughter weight is clear (Johnson-Ifearulundu and Kaneene, 1997). Vandehaar et al. (1995) found that negative energy balance can reduce the development of *corpus luteum* with consequent reduction of the serum progesterone level.

3.3.2. Impaired cellular immunity

The association between cellular immunity and increased risk of occurrence of secondary diseases has been described by Kreeger et al. (1992). It is supposed that persistence of the disease in an organism may cause an inadequate immune system cell response (Kreeger et al., 1991, 1992). Kreeger et al. (1991) found that infected cattle monocyte response to antigens is reduced. An association between *MAP* infection and reduced immunocompetence may be the basis for the elevated rate of culling due to mastitis, infertility and other health problems (Johnson-Ifearulundu and Kaneene, 1997).

4. The impact of paratuberculosis on milk production

PTB is one of many factors associated with intra-herd variance in milk production. Others factors include genetic ability to produce milk, as well as a variety of environmental factors, such as management of feeding and milking systems (Weigel et al., 1993). The association between the production potential and probability of culling due to PTB was detected when highly productive cows which were infected with *MAP* were shown to be more likely to develop clinical disease (Benedictus et al., 1987; McNab et al., 1991b).

Decreased milk production has been described in several studies; different authors estimated the

consequences from various aspects by different methods. PTB has been documented to reduce milk production in infected dairy cows with clinical signs of the disease and without apparent clinical signs (Buergelt and Duncan, 1978; Abbas et al., 1983; Whitlock et al., 1985; Benedictus et al., 1987; Johnson-Ifearulundu et al., 1999; Ott et al., 1999). However, reported losses are inconsistent, ranging from 2.2 to 25.0% of annual herd production.

Dufour et al. (2004) focused their study on the reduction of milk production in animals affected with both clinical and subclinical forms of this disease. They found that the expense caused by milk production loss in clinical cases is additional to the other expenses in dairy herds. The degree of these losses depends on the time of initiation of the disease. In cases where clinical signs appear soon after calving, production is lost for the whole lactation period. Annual expenses per one subclinically infected animal in a dairy herd have been calculated as the corresponding amount of production lost by the price of a litre of milk.

4.1. Methods of estimation of milk production losses

Various methods of lost milk production estimation have been used in respective studies.

4.1.1. Estimation according to Benedictus et al. (1987)

Benedictus et al. (1987) evaluated milk production losses in Friesian-Holstein breed in the Netherlands. Their study included 61 animals with manifested clinical signs, originating from 11 farms and further 52 animals without clinical signs, originating from 7 farms. They determined the percentage of decreased production in lactation when culling was performed with respect to the previous lactation using the following formula:

$$100 - (LL/[LL - 1] \times 100)$$

where:

LL = milk production in the lactation during which culling was performed

$LL - 1$ = milk production in the previous lactation

Estimated production losses during all lactations were used for determination of a number of affected lactations. Their estimation was performed with respect to production in the first lactation. They found that, in a group of animals with clinical PTB, that milk production in the last lactation and in the previous lactation was decreased by 19.5% and 5%, respectively. In animals without apparent clinical signs, milk production in the last lactation and in the previous lactation decreased by 16% and 6%, respectively.

4.1.2. Estimation according to Buergelt and Duncan (1978)

Buergelt and Duncan (1978) investigated changes in milk production of 80 cows of Friesian-Holstein breed in the USA. They recorded 16% and 6% reduction of milk production in the last lactation in cows with and without clinical signs of PTB, respectively. Another method of estimation of milk production losses was used in their study. Milk production of the culled animals was classified in three groups according to the status of infection, which was evaluated in pounds (lb) where 1 lb = 0.45 kg:

(i) The first group included PTB-free animals with milk production of 17 206 lb.

(ii) The second group included animals with clinical PTB (persistent incurable diarrhoea and body weight loss) with milk production of 14 470 lb.

(iii) The third group included animals affected by PTB without clinical signs (as confirmed by culture or gross examination) with milk production of 15 873 lb.

The average milk production in groups 2 and 3 was compared with control group 1 using the Dunnett *t*-test. The difference between group 2 and control group was significant at the level of 5%. The difference between group 3 and control group was not statistically significant.

4.1.3. Estimation according to Kormendy et al. (1989)

Kormendy et al. (1989) investigated 500 cows of Jersey × Holstein-Friesian breed in Hungary. In their three-year study they estimated a total annual milk production (for respective years of investigation) as a percentage of national annual average milk production. In the first, second and third year of diagnosed PTB, the annual milk yield per cow was decreased by 49 l, 474 l and 1 030 l, respectively, whilst in previ-

ous years, annual average milk production oscillated around the national average.

4.1.4. Other methods of estimation

In a New Zealand study, milk production losses varied from less than statistically significant in slightly infected herds up to a 17% reduction in the most seriously affected herds (De Lisle and Milestone, 1989). Abbas et al. (1983) recorded a 15% (1 838 lbs) reduction in the annual average milk yield from subclinically infected cows in comparison with control (*MAP*-non-infected) cows. In this study it was found that the association between *MAP*-infection and poor performance in reproduction and production was statistically significant.

Wilson et al. (1993) estimated the loss of milk production in animals affected by PTB after the second lactation to range between 1 300 and 2 800 lbs per lactation. This loss of milk production to the producers represented USD 80 to 250 per lactation (Wilson et al., 1995). The expenses varied between respective lactations, from no significant effect in the first lactation to a loss of 250 USD/cow/year in the fourth lactation.

Nordlund et al. (1996) published that *MAP*-infected cows in Wisconsin produced from 2% to 19% less milk than their herdmates. The loss to the dairy industry caused by subclinical PTB was estimated using the national average milk production of 6 704 kg of milk per cow. The loss was presented as 6.5 million kg of milk per year with a total cost of about USD 1.85 million.

A study performed by Norlund et al. (1996) in Wisconsin, differs from the other studies of milk production by the number of examined herds (i.e. 23). The differences in milk production between infected and non-infected cows were highly variable between respective herds. It was not clear why the results between herds differed; however, it might have been caused by the *MAP* strain type that infected each of the herds, or by interactions between *MAP* and the management system in respective farms. Another possible cause of this between-herd variation might have been the infection of animal subpopulations with different genetic production potentials within a herd.

The study of Lombard et al. (2005) also comprised a large number of animals (more than 27 000 cows from 38 herds); however, they evaluated milk production in each cow separately and did not compare respective herds. They found that cows with strongly positive results of ELISA had ME 305-day milk production, ME 305-day maximum milk production and total lifetime milk production significantly lower than negative cows. ME 305-day milk production was reduced by approximately 3 000 lb, maximum ME milk production was reduced by 1 204 lb (4.9%) and lifetime total milk production was reduced by 10.8%.

In contrast to the above mentioned studies on animal models, Groenendaal et al. (2002) and Groenendaal (2005) used the simulation model – JohneSSim for the evaluation of milk production and other losses. It is a model that takes into consideration the herd dynamics of this disease, control of PTB and the above mentioned economic consequences. It is based on literature data and proposals of experts and it has been evaluated for a period of 20 years. According to this model, losses of milk production are related to the infection state: 5% (lowly infectious) and 20% (clinical).

The use of the simulation model has several potential advantages (comparability and dynamics) over the studies on living models – herds. However, it has also several disadvantages, such as it does not take into consideration the increased frequency of secondary diseases, trade restrictions etc.

4.2. The extent of losses and parity at culling

The amount of milk produced at 200 days averages about 80% of the expected annual total milk production (Dijkhuizen, 1980, as quoted by Benedictus et al., 1987). Benedictus et al. (1987) found that animals with both clinical and subclinical PTB were culled at an average of 200 days into the lactation. According to another study, clinical signs appeared in 90% of diseased cows soon after calving; it follows that the total annual production was lost. The disease began to be apparent later during lactation in other clinical cases with corresponding loss of a part of the annual production only (Dufour et al., 2004).

4.3. Economic impact of respective diagnostic methods

One of the major factors influencing production loss estimates associated with PTB is the diagnostic

test that is used to discriminate infected from presumed non-infected animals (Hendrick et al., 2005). In a study of two herds in Ohio (USA), *MAP*-positive cows, as determined by faecal culture results, produced 18.8% less milk than did *MAP*-negative herdmates (Spangler et al., 1992). However, significant differences in milk production were not found between *MAP*-positive and *MAP*-negative cows in the same herds when diagnosis was made by enzyme-linked immunosorbent assay (ELISA).

Other milk production studies have not been reported on the basis of the USDA-licensed *MAP*-ELISA, but a study based on results of a Lipoarabinomannan (LAM)-ELISA did not indicate a significant milk production difference between test-positive and test-negative cows (McNab et al., 1991a).

Production effects associated with PTB-positive status will differ with the diagnostic test used because diagnostic tests differ in accuracy and stage of infection detected. For example, comparison of ELISA and faecal culture results for the same *MAP*-infected animals by use of the kappa statistics indicated that the two tests detected different subgroups of animals (Collins et al., 1991). Likewise, the LAM-ELISA detected different subgroups of animals than did an agar gel immunodiffusion test (AGIDT) and a complement fixation test (CFT) for PTB (McNab et al., 1991b).

Nordlund et al. (1996) detected that the mature equivalent (ME) of milk production was 376 kg per lactation lower in ELISA-positive cows in comparison with ELISA-negative cows. The results of this study showed that subclinical *MAP* infection diagnosed by USDA-licensed *MAP*-ELISA was associated with an average 3.95% (ranging between 1.44 and 6.46%) reduction in milk production. The study revealed only the association, not the cause of these losses.

Hendrick et al. (2005) in their study investigated and compared results of three diagnostic tests (faecal culture, milk ELISA and serum ELISA) and milk production. They found that cows with positive results of bacteriologic culture of faeces or milk ELISA produced 457 or 548 kg less milk in a 305-day lactation compared with negative herdmates. Similar associations were found between results of bacteriologic culture of faeces and milk ELISA test status and 305-day fat and protein production. The only association found for cows with positive results of the serum ELISA was a significant reduction in 305-day protein production, compared with sero-negative cows.

Most tests for PTB have high specificity but low sensitivity which results in a very small proportion of non-infected animals being falsely classified as positives and a high proportion of infected animals being falsely classified as negatives. An outcome of these misclassifications is that production differences between test positive and negative animals and herds will underestimate the actual losses. As infected animals are more likely to test positive late in the course of the disease, the measured losses more accurately reflect those associated with advanced infection.

On the other hand, Johnson et al. (2001) assumed that the key to the inconsistent results presented in the literature regarding subclinical *MAP*-infection and milk production might not be in the method of diagnosis but in the parity of the cows in the study.

4.4. Milk production losses and effectiveness of control programmes

An accurate estimate of subclinical production losses is an important factor in assessing the cost-effectiveness of PTB "test-and-cull" programs (Collins and Morgan, 1991). If subclinical *MAP* infection reduces milk production at the highest rate reported, "test-and-cull" programs are probably cost-effective, even in herds with extremely low prevalence. However, if milk production losses are minimal, "test-and-cull" programs become cost-effective only in herds with high prevalence. The losses of milk production under 6% are viewed by the authors as minute losses and they suggest that the factors such as herd size, contact of adult animals with calves and the level of herd milk production have a little effect on profitability and "test-and-cull" programme.

In contrast, Groenendaal et al. (2002) suggest that improved calf management including preventing calves from contact with adult animals should be an inseparable part of each control programme that should lead to an increased effectiveness. Some authors also believe that extreme variability in losses caused by PTB between respective farms is based on differences in prevalence, management system and farm size (Benedictus et al., 1987; Ott et al., 1999).

The short-term economic losses associated with premature culling of test-positive animals that have yet to experience declines in milk production, must

be weighed against the risk of further environmental contamination and spread within the herd that is posed by keeping subclinically infected animals within the herd. Increasing the herd prevalence of PTB positive animals may result in greater long-term economic losses (Hutchinson, 1996; Johnson et al., 2001).

Milk production losses should not be isolated from the other losses; however, a complex approach to the evaluation of control programme effectiveness is necessary. The method "test-and-cull" should primarily ensure disclosure and culling of positive animals with consequent decrease not only in milk production losses. It is necessary to combine this method with the tools of management improvement (Groenendaal and Galligan, 1999; Groenendaal, 2005).

4.5. Milk constituents (fat and protein)

Knowledge of the association between milk constituents and PTB is scarce and inconsistent. Significant difference was not found in lactation average percentages of fat and protein. The "lactation percentage" (LA%) of fat content ranged between 2.51 to 5.31 and 2.06 to 6.80 in *MAP*-positive and negative cows, respectively. The LA% protein content ranged between 2.58 to 3.73 and 2.43 to 4.42 in *MAP*-positive and negative cows, respectively (Nordlund et al., 1996).

The studies of Johnson et al. (2001) and Lombard et al. (2005) did not show significant differences in milk fat and protein content between *MAP*-positive cows and their negative herdmates. In contrast Sweeney et al. (1994) published that daily milk fat and milk protein production were significantly less for the infected cows. Collins and Nordlund (1991) reported that subclinical PTB was associated with a reduction in 305 day mature equivalent protein and fat that costs producers USD 205 per cow per lactation.

4.6. Mastitis

Merkal et al. (1975) found that PTB has been associated with increased mastitis culling; that was confirmed by McNab et al. (1991a). In one of the investigated herds, mastitis was the reason for culling 3.6% of the non-infected and 22.6% of the infected cows with unapparent PTB (Merkal et al., 1975). Buergelt and Duncan (1978) documented that culling was more frequently attributable to mastitis in a group of animals with subclinical PTB (27.3% cows) than in control group of *MAP*-non-infected animals (6.6% cows).

Wilson et al. (1993) gave evidence of a positive correlation between *MAP*-positive status and lower prevalence of mastitis. Two years later they reported that PTB was associated with economic benefit due to lower rates of mastitis in positive cows, but a net financial loss resulted because of reduced milk production and increased culling rates (Wilson et al., 1995). In contrast, De Lisle and Milestone (1989) failed to find any association between *MAP* infection status and mastitis.

4.6.1. Mastitis pathogens in infected cattle herds

Wilson et al. (1993) investigated not only the infectious status of cows with respect to *MAP* infection, but also examined quarter samples for potential presence of mastitis pathogens. No causative agents of mastitis were isolated from the majority of cows (*MAP*-positive and negative) but more mastitis pathogens were isolated from milk of *MAP*-negative cows. This association between *MAP*-positive status and a lower prevalence of mastitis was significant (x^2, $P < 0.05$).

Staphylococcus aureus was detected in 84 *MAP*-negative cows, i.e. significantly more (x^2, $P < 0.001$) than in *MAP*-positive cows (4 animals only). Significantly more *MAP*-positive cows were affected with mastitis caused by coagulase-negative *Staphylococcus* sp. in comparison with their negative herdmates (x^2, $P < 0.001$). *Serratia* sp. mastitis was only diagnosed in *MAP*-negative cows.

4.6.2. Somatic cell counts

McNab et al. (1991a) gave evidence that subclinical *MAP*-infection in cows in Canada was associated with increased somatic cell count (SCC). In contrast, Spangler et al. (1992) did not confirm the association between SCC and *MAP*-infection in the USA one year later. Another year later, Wilson et al. (1993) documented in the USA that SCC was lower in *MAP*-infected cows up to the third lactation when in contrast, this value was higher. Ten years later, Chaffer et al. (2002) did not find a

statistically significant difference in SCC between subclinically *MAP*-infected and *MAP*-non-infected cows in Israel.

McNab et al. (1991b) demonstrated that LAM-ELISA positive results were associated with higher milk SCC, the herd average, and individual cow levels of organization. However, the last study conducted in the USA (Lombard et al., 2005) did not reveal significant differences in SCC between *MAP*-infected and *MAP*-non-infected cows. According to Hutchinson (1996) different results obtained by investigation of PTB effect on SCC (and fertility) may be associated with sensitivity of the used diagnostic tests and with differences in the stage of development or severity of infection in the test-positive animals.

5. The disease and fertility

There is no proof that fertility and PTB are related, but this possibility must not be overlooked as infertility has an important impact on the economics of dairy farming (Stott et al., 1999). Kopecky et al. (1967) published noteworthy results concerning *MAP* isolation from uterine wall and ileocaecal valve mucosa in a herd where sterility of cows was the major problem and reason for culling. They evaluated the results together with the reasons for culling of 23 cows from the herd; *MAP* was detected in the ileocaecal valve only from 15 animals, and in either of the tissues from 8 culled animals.

One potential source of economic losses in subclinically infected cows is reduced fertility (Johnson-Ifearulundu et al., 1996). Infertility was significantly higher in cows with unapparent *MAP*-infection than in non-infected cows in the same herd (Merkal et al., 1975). Buergelt and Duncan (1978) have shown that cows with subclinical *MAP*-infection frequently had infertility problems.

5.1. Nutrition status and reproductive efficiency of cows

One of the supposed mechanisms of decreased fertility of cows is based on the association between nutrition status and reproductive efficiency (Johnson-Ifearulundu et al., 2000). It has been reported that negative energy balance (inadequate dietary energy intake) can reduce growth and development of *corpus luteum* and result in a reduction of the serum progesterone (Vandehaar et al., 1995).

5.2. Methods of estimation of decreased reproductive efficiency

Two studies have found that cows subclinically infected with *MAP* are at a greater risk of being culled for infertility (Merkal et al., 1975; Buergelt and Duncan, 1978). A third study reported that subclinically infected cows have a 1.73 month increase in calving interval compared to non-infected cows (Abbas et al., 1983). The duration of this period was 15.18 months in *MAP*-infected cows and 13.45 months in *MAP*-non-infected cows. However, other studies have failed to find an association between subclinical PTB and infertility or calving interval (De Lisle and Milestone, 1989; McNab et al., 1991b) and comparison between inter-calving interval of the two groups (*MAP*-infected and *MAP*-non-infected animals) showed no significant differences (Chaffer et al., 2002).

Johnson-Ifearulundu et al. (1996) focused in their study on the impact of subclinical *MAP*-infection on the number of days from parturition to conception (days open). This period was statistically significantly ($P < 0.05$) longer (141.5 days in average) in *MAP*-infected cows than *MAP*-non-infected cows (104.5 days in average). Their further study (Johnson-Ifearulundu et al., 2000) brought comparable results: ELISA-positive cows had a 28-day increase in days open when compared to ELISA-negative cows ($P = 0.02$).

Kormendy et al. (1989) used the conception index, calving rate and foetal and *post partum* calf losses (abortions, stillbirths, and *post partum* deaths) for the assessment of reproductive efficiency status. The losses were expressed in percentages of the total annual calf number, including aborted and stillborn calves. The pregnancy and calving rates were at the usual level during the years of the study. Total calf losses increased from 9 to 16% during the five-year period and were over the national average. While calf losses due to death increased from 0.6 to 7.3%, the percentage of losses due to abortion and stillbirth did not change during the study. Cvetnic et al. (2002) gave evidence that parturition is usually normal but the foetus is often smaller and 30% lighter.

6. The loss of genetic value of animals

The loss of genetic value of animals through premature culling (Johnson et al., 2001) and through trading restrictions is one of less evident losses. Opportunities to sell animals with a high genetic value from infected herds are limited (Kennedy and Benedictus, 2001).

7. Feed conversion and decreased slaughter value of animals

Despite milk production decline in *MAP*-infected cattle herds, feed consumption does not change. It is caused by maintained appetite of infected animals, although feed conversion gradually decreases due to chronically affected intestinal mucosa (Ott et al., 1999).

In contrast to this information, Benedictus et al. (1987) considered a decreased consumption of feed by ill animals in the calculation of production losses before culling and they took a certain amount of non-consumed feed from total expenses. However, the appetite remains good in PTB, even in the clinical stages (Doyle, 1956).

Kormendy et al. (1989) estimated the total annual consumption for each year of a 3-year (1982–1984) investigation. Feed efficiency was expressed by feed conversion per one litre of produced milk. In 1977, before the outbreak of PTB in the herd, feed conversion was 61% related to hypothetical 100% conversion; after the outbreak of PTB it was gradually decreased during the three years of the investigation from 45% to 44% and 39%, respectively.

The weight loss, which contributes to the reduced slaughter value, is caused by malabsorption and protein losing enteropathy. Proteins losing enteropathy (Patterson et al., 1967) and intestinal malabsorption (Patterson and Berrett, 1968) have been reported in association with PTB. Enteropathy and malabsorption can result in reduced feed efficiency and poor weight gain. These effects appear not only in clinically ill animals, but also in subclinical cases (Johnson-Ifearulundu et al., 1999). Decreased slaughter weight at culling has been reported for clinically (Benedictus et al., 1987) and subclinically (Merkal et al., 1975) *MAP*-infected animals. A 10% increase in the proportion of cows positive for PTB was associated with a 33.4 kg (73.5 lb) decrease in mean weight of culled cows (Johnson-Ifearulundu et al., 1999).

Slaughter value of a culled dairy cow in typical body condition was estimated to be USD 400 per head and USD 250 (38% reduction) per head for a poor-condition cull (Ott et al., 1999). Groenendaal et al. (2002) estimated by means of a simulation model (JohneSSim) that the reduction of slaughter value ranged between 5% (lowly infectious) and 30% (clinical).

8. Decreased production age of animals

Mortality rate and numbers of culled animals are increased in an infected herd (Ott et al., 1999). Economic consequences caused by increased mortality rate may be expressed as a lost slaughter value of dead animals and expenses for purchasing replacement heifers. Economic expenses caused by culling the animals includes decreased slaughter value, expenses for purchasing replacement animals and above all unrealized future income and expenses for idle production.

8.1. The reasons for culling of animals from a herd

Buergelt and Duncan (1978) documented in a group of *MAP*-infected animals with clinical signs that the primary reasons for culling were culture of faeces (50% animals), body wasting (33% animals) and decreased milk production (17% animals). The reasons for culling in the group of *MAP*-infected animals without clinical signs were the following: low milk production (46% animals), mastitis (27% animals), infertility (9% animals), positive culture of faeces (9% animals) and positive CFT (5% animals). The primary reason for culling of non-infected cows was low production (47% animals), age of the animals (20% animals), infertility (13% animals), mastitis (7% animals) and body wasting (7% animals).

In the study of Johnson-Ifearulundu et al. (1999) a 3% increase in herd mortality rate associated with PTB was found. This association reflects deaths directly caused by PTB with deaths attributable to an increased risk of secondary disease. Kreeger (1991) reported that annual death losses may range from 3 to 10% in an infected herd.

8.2. Increased predisposition to other diseases

Impairment of cell-mediated immunity in PTB-infected animals has been proposed to increase the risk of secondary disease (Kreeger et al., 1992).

Polymorphonuclear neutrophils migration (PMN) (unstimulated or stimulated cells with zymosan-activated serum) was investigated in the study of Dotta et al. (1999). They detected significantly lower PMN (after stimulation) in cows with subclinical PTB in comparison with uninfected cows. Migration of unstimulated cells in the infected cows did not differ from that in the uninfected cows. It seems that the infection influenced only the migratory cells.

Association between PTB and increased risk of secondary diseases has also been described by other authors (Johnson-Ifearulundu et al., 1999; Kennedy and Benedictus, 2001).

8.3. The disease and the average age of cows

Merkal et al. (1975) reported that animals in their study (without clinical signs in a farm, where no control programme has been established) had a short life expectancy. The average age of all the animals culled in the study of Benedictus et al. (1987) was 5.66 years. This is not consistent with the findings of Merkal et al. (1975).

The association between average age of cows and diagnosed PTB in a herd of dairy cows was investigated by Kormendy et al. (1989). After the detection of PTB in the surveyed dairy herd, the average age decreased from 63.9 to 57.0 months. The authors presented the age structure of a production herd. The results indicated decreasing productive age of the animals. Buergelt and Duncan (1978) documented decreased production age of the infected cows in comparison with their non-infected herdmates. The age of infected cattle was significantly lower than non-infected cattle indicating infected cattle had a shorter life expectancy.

8.4. Premature culling and unrealized future income

In animals in good health and with normal production potential, the average income increases with age (Dijkhuizen et al., 1985). The greatest economic loss was attributed to unrealized future income caused by premature culling of infected cattle (Benedictus et al., 1987). These losses were estimated to be 43%.

According to the Groenendaal and Galligan (2003) study most of the loss (>70%) attributable to PTB was categorized as a loss of future income. However, both losses of future milk production and expenses for replacement of a cow were included in their simulation model. Normal loss is determined by the age at culling and the production potential of the animal. The lost production potential may be estimated on the basis of the production in the first lactation relative to the herd average. The average unrealised future income for an average production level of 108% of the herd was 279 GBP (Benedictus et al., 1987). Cows with a higher production potential were more likely to be culled because of PTB (Benedictus et al., 1987; McNab et al., 1991b). High producing cows were frequently culled after their first or second gestation, contributing to an undetermined economic loss with regard to their potential breeding value (Buergelt and Duncan, 1978).

Many animals were slaughtered at a relatively young age and before they reached the peak of their lactation potential (Hutchinson, 1996). Some young cows had outstanding milk production data when they were taken from the herd. The loss in breeding value added another economic component. The study of Wilson et al. (1995) reported that the culling rate was greater for PTB-positive cows during all (four) lactations, with culling losses of approximately USD 75 per cow per year.

9. Expenses for herd replacement

Expenses for herd replacement result from increased mortality rate and increased culling rate of animals due to PTB or other reasons associated with PTB (Johnson-Ifearulundu et al., 1999).

9.1. Losses resulting from culling of animals

The animals culled because of PTB are replaced by the purchase of pregnant heifers, and the losses induced by the culling of a sick cow are thus estimated by the price of a pregnant heifer. For the average dairy herd, the losses induced by the culling of a female calf were estimated by half (50% of the calves being females) of the margin made on an 8-day old veal calf (Dufour et al., 2004). For example, Kreeger (1991) assumed the replacement heifer cost to be about USD 1 100.

9.2. Expenses resulting from idle production

When an animal is culled there is often a period when a replacement animal is not immediately available (Benedictus et al., 1987). The expenses increase on one hand because the operation costs for the whole herd remain; on the other hand, the income decreases because the production of the lost animal has not been replaced yet.

10. Control costs

The costs of controlling PTB consist of the costs of veterinary services, costs of diagnostic testing programmes and the costs of management changes instituted by the farmer (Kennedy and Benedictus, 2001). Wilson et al. (1993, 1995) gave evidence that culling only based on positive culture of faeces in a dairy herd with a high prevalence of PTB is unwarranted and expensive. Test-and-cull programs alone do not reduce the PTB prevalence and are on average economically unattractive. The average costs of the different test-and-cull strategies were higher than the benefits of the programs (Groenendaal, 2005).

Groenendaal and Galligan (2003) used a simulation model (JohneSSim model) for the estimation of control costs; that assessed losses under certain conditions during the past twenty years. Mean loss increased considerably from 35 USD/cow/year in year 1 to >72 USD/cow/year in year 20.

10.1. Expenses for diagnostic testing programmes

Expenses for diagnostic testing programme represent a substantial part of total expenses (Collins and Sockett, 1993).

Collins and Sockett (1993) compared six diagnostic methods and found that their costs ranged between USD 2.36 per ELISA test and USD 24.65 per DNA probe. An optimum diagnostic test has to be available for the lowest price and showing the highest specificity. High specificity minimizes the number of false-positive results and consequently the number of unnecessarily culled animals (Collins and Sockett, 1993). It is the owner who must bear the economic consequences resulting from false-positive and false-negative diagnostic test results.

At 70 NOK (1 USD = 7.9 NOK) per test, the initial cost of testing would be approximately 5 million NOK. In addition, it was assumed that any herds that were classified as *MAP*-sero-positive would be re-tested. A herd was classified as infected if one or more *MAP*-sero-positive animals were found; the median cost of detecting a truly infected herd was approximately 900 000 NOK (Paisley, 2001).

10.2. The time necessary to put paratuberculosis under control

The analysis revealed that use of the ELISA required 11 years to achieve eradication, but was the least expensive in total testing costs. Conventional culture in parallel with the ELISA was the next least expensive testing system for PTB eradication (Collins and Sockett, 1993).

10.3. Costs of changing the management

Expenses for the management changes and improved standard of hygiene are inseparable parts of control expenses (Groenendaal and Galligan, 1999; Kennedy and Benedictus, 2001); their purpose is to reduce the exposure of calves and older animals to the causative agent of PTB and hence to decrease prevalence of PTB in a herd. For instance the use of milk replacer over whole milk is an economically very attractive control tool.

It is difficult to estimate these expenses; they are highly variable between respective farms (Hutchinson, 1996; Groenendaal and Galligan, 1999). Management steps to prevent calf exposure to PTB may also reduce exposure to pathogens such as *Salmonella*, *Escherichia coli*, cryptosporidia and coccidia (Hutchinson, 1996; Groenendaal and Galligan, 1999). Without management changes designed to reduce the farm-level prevalence of *MAP* infection, PTB will continue to reduce farm income by decreasing milk production and increasing premature culling from the herd (Lombard et al., 2005).

11. Export and import restrictions

The herds with positive reactors (in ELISA test; infected or not) would be placed under movement

and trade restrictions until the diagnosis could be confirmed or rejected (Paisley, 2001). Animals from farms or areas known to be infected may suffer price penalties or may sell only for slaughter (Kennedy and Benedictus, 2001). Certain trade restrictions lead to losses at a national and international level. States suffer losses due to the cost of control programs, loss of revenue from lost income, and trade restrictions between certain states (Whipple, 1991).

12. Losses at state level and farm level

Various authors estimated a total financial loss caused by PTB in different states. The approach of respective authors differed from an aspect of items (losses) included in the resulting total financial loss. In Wisconsin, the estimated cost of PTB was nearly USD 52.395 million annually. The loss of efficiency (USD 25.865 million) and the loss caused by clinical disease (USD 26.529 million) were included in the total loss. Later studies estimated this loss to dairy industry to be USD 100 million annually (Sockett, 1996).

Subclinical disease alone costs the state of Wisconsin (USA) USD 1.85 million per year in reduced milk production (Nordlund et al., 1996). Losses in Pennsylvania (USA) were estimated to be more than USD 5.8 million annually (Whitlock et al., 1984). Besides the loss of milk production (USD 5.2 million), the loss of body weight and consequently slaughter value (USD 0.648 million) were included in the total loss.

Chiodini and Van Kruiningen (1986) estimated the economic impact of PTB in the New England (USA) area to be more than USD 15.4 million annually. Slaughter value, farm value, economic losses due to clinical PTB and economic losses due to decreased productivity were included in this study.

Meyer and Hall (1994) using two different methods obtained similar results. They estimated the annual loss to be USD 4.5 million for the dairy industry in Kentucky (USA). Loss of income and cull value of infected dairy cows which are culled (USD 3.5 million) and loss of income and cow value of infected dairy cows which die (USD 1.0 million) was included in this sum. The losses in beef cattle were only USD 1.5 million.

The greatest economic impact of PTB is at the individual farm and herd owner level (Whipple, 1991). The impact of infection varies with each farm depending on management practices used to control the disease. Quarantines and certain trade restrictions may make the economic impact of having infected cattle on a farm greater than the actual losses due to the disease. The economic costs to a positive herd from lost breeding value and lost trade as states and countries impose restriction on the transport and sale of cattle from PTB-positive herds may be exceedingly difficult to determine on the individual herd-level (Jones, 1989).

Producers who openly attempt to control PTB in their farm and do not transmit it to other farms, bear an unrighteous burden caused by current restrictions in comparison with farms where diagnostic testing is not performed, either knowingly or unknowingly (Johnson-Ifearulundu and Kaneene, 1997).

More accurate estimates of the true losses associated with PTB will be possible with better quantification of effects on milk production, mastitis, reproduction, other diseases, culling and lost genetic value in infected herds.

13. Conclusions

Economic losses caused by PTB in dairy cattle herds represent a significant but often unrecognised burden both to farmers – the owners of infected herds – and dairy industry of a particular state. However further studies of economic consequences attributable to PTB is necessary to properly evaluate disease control programmes, programmes of certification of PTB-free herds and above all for improvement of the situation of farmers who are owners of infected herds.

This review article presents potential impact of PTB on dairy cattle herds. The majority of studies showed an association between PTB and decreased milk production. According to some authors (McNab et al., 1991b; Spangler et al., 1992; Nordlund et al. 1996; Hendrick et al., 2005), the extent of milk production decline was associated with the respective disease classification methods used. This fact reflects differences between respective tests and of course also the stages of infection.

The authors of the present study agree with Hutchinson (1996): "Further studies are needed to identify the onset and progression of milk-production effects of PTB relative to detectable culture and/or serologic-positive status."

The effect of PTB on milk production should be considered as a whole, together with other factors

such as environmental factors. The effect of PTB on milk fat and milk protein levels should also be considered together with a number of other factors. Hendrick et al. (2005) view PTB as one of many factors that influence milk production and culling.

The impact of PTB on mastitis (and also on SCC) has not been fully clarified yet. Some authors found associations between PTB and increased mastitis-based culling of animals from a herd. In contrast, a low prevalence of mastitis or no association was detected in other studies. Further investigation of this subject should be performed with the aim to confirm or exclude involvement of PTB.

It follows from the present review that it is preferable to prevent transmission of *MAP* among cattle herds as its subsequent control is very expensive and long-lasting (Pavlik et al., 2000c). Due to the fact that non-significant statistical differences in the distribution of the causative agent of PTB within the organism of various dairy, beef and dual-purpose cattle breeds were found (Pavlik et al., 2000b), we believe that PTB may also cause high economic losses in the herds of beef and dual-purpose cattle herds.

Economic losses may increase in *MAP*-infected herds due to an increasing number of studies focused on the hypothesis that there is a causal association between *MAP* and a Crohn's disease (Thompson, 1994; Hermon-Taylor et al., 2000; Hruska et al., 2005). These economic effects may be caused by milk price reduction as a consequence of consumers' fears. Groenendaal and Galligan (1999) indicated that in case this situation comes, the losses may be so high that a national PTB eradication programme will be economically attractive.

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