Mycobacterium avium ssp. *paratuberculosis* in milk: risk considerations*)

Von P. Hammer

Institute for Hygiene and Food Safety, Federal Research Centre for Nutrition and Food – Location Kiel, P.O. Box 6069, D-24121 Kiel

1. Introduction

Information on the significance of *Mycobacterium avium* ssp. *paratuberculosis* (*M. paratuberculosis*) for animal health, consumer health, and for processing including heat resistance can be used within the Codex Alimentarius approach on microbiological risk analysis. In the sense of the principles and guidelines elaborated by the Codex Committee on Food Hygiene (1) microbiological risk analysis is a three-step procedure consisting of risk assessment, risk management and risk communication with the objective to ensure public health protection (2) (Figure 1).

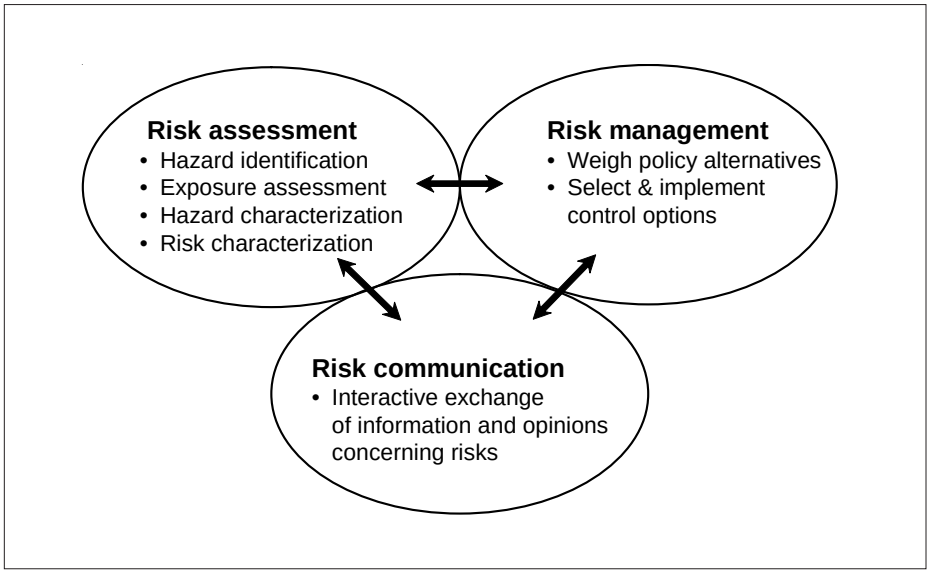

Fig. 1: Codex Alimentarius approach on microbiological risk analysis, modified from LAMMERDING 1996 (2)

*) Updated paper originally presented at the conference "Mycobacterium paratuberculosis", organized by the Society of Chemical Industry, Food Commodities & Ingredients Group at the Queens University, Belfast, April 10, 2002

A microbiological risk assessment (RA) in this framework will, e.g. result in an estimate of the prevalence of an illness or an estimate of the incidence of an illness, or an estimate of the rate of human illness and severity per serving. It must have a sound scientific basis, and should be structured in four steps:

- hazard identification
- exposure assessment
- hazard characterization
- risk characterization

Although a formal RA according to the Codex procedure is not yet feasible for *M. paratuberculosis* the structure of the procedure can be followed. It must be noted that RA in the sense of the Codex approach leads to an estimate for a population or at least a part of it. It must not be confused with hazard analysis in the framework of HACCP, which may also lead to a risk estimate, however, only at the level of the analyzed process.

2. Hazard identification

Risk assessment starts with the hazard identification. This is a qualitative process aiming at the identification of microorganisms (or their toxins) of concern and the evaluation if they represent a potential hazard when present in food (1).

As long as the discussion whether there is an association between *M. paratuberculosis* and Crohn's disease of humans is still open this process can not be finalized. The present state of the art is published in three papers, which are of relevance and which in addition mention the need for more research to come to a final decision.

- The Scientific Committee on Animal Health and Welfare of the European Commission concludes in its report dated March 2001 (3): "The currently available evidence is insufficient to confirm or disprove that *M. paratuberculosis* is a causative agent of at least some cases of Crohn's disease in man. There are sufficient grounds for concern to warrant increased and urgent research activity to resolve the issue."
- A report for the Food Standards Agency (4) dated June 2001 states: "For the present all that can be said with certainty is that there is not enough data available on the incidence and prevalence of the two diseases (Johne's disease and Crohn's disease) both in time and geographically to enable any conclusions on correlations or causality to be made. While such studies are urgently needed they will not be easy to develop or to interpret, and they will take several years to produce results. They need to be internationally coordinated if they are to be as informative as possible."
- The German Federal Institute for Health Protection of Consumers and Veterinary Medicine conducted an expert consultation on microbiological risk assessment of a link between *M. paratuberculosis* and Crohn's disease in September 2001. The experts discussed the role of the bacterial flora in inflammatory bowel diseases in detail and concluded that the question whether *M. paratuberculosis* is a causal agent in Crohn's disease or is just occurring in coincidence is still open. There is no evidence from the existing data that the organism is a monocausal agent for Crohn's disease, however, it cannot be excluded that mycobacteria in general contribute to a perpetuation of the inflammatory processes. Even if *M. paratuberculosis* only plays a minor role for a small subgroup of CD patients it is of relevance for food hygiene (5).

Summarizing these papers and considering a position as defined in the “Greenbook on Principles of Food Laws in the European Union“ it can not be excluded that *M. paratuberculosis* may adversely affect human health because there is still uncertainty whether it is at least one factor in Crohn’s disease (maybe only in a subpopulation of patients). In cases where the scientific basis is insufficient or some uncertainty exists the risk analysis of the Commission will be guided by the precautionary principle. This precautionary principle has been laid down in a regulation of the EU (178/2002) on “general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety“ (6). Thus, according to the Greenbook and regulation 178/2002 precautionary measures must be applied with respect to the safety of the consumers – and as long as there is any uncertainty *M. paratuberculosis* must be presumed as a hazard in the sense of hazard identification.

3. Exposure assessment

Exposure assessment is a process resulting preferably in a quantitative estimate of level and likelihood of the occurrence of a pathogen in a certain food including the level of uncertainty. This estimate will be the expression of the extent of actual or anticipated human exposure (1). Considerations for the quantitative process, e.g. include:

- extent of food contamination (frequency, level, initial contamination, preparation steps with respect to reduction)
- unit of food of interest, portion size (in case of illness)
- patterns of consumption
- mishandling, potential for recontamination
- pathway from production to consumption
- scenarios to predict range of possible exposures

If only a qualitative estimate is possible, one should consider the likelihood of a food being contaminated at its source, the support of growth in the food, potentials for abusive handling, and eventual heat processes.

3.1 Prevalence in raw milk

The prevalence of *M. paratuberculosis* in raw milk is mainly influenced by the health status of the cow including endogenous spread of the organism but also faecal contamination during milking.

Data from the literature presented here do consider only incurred *M. paratuberculosis* (Table 1). Shedding of the organism with the milk was detected in clinically diseased cows and in subclinically diseased cows close to a clinical onset of disease. The only quantitative estimate is given by Sweeney et al. (7). These authors detected 2-8 cfu/50 ml raw milk.

The faecal contamination route during milking is not considered here although it might be the most important one in practice (this will be discussed later).

Tab. 1: Prevalence of *M. paratuberculosis* in raw milk

Diseased cows	subclin. inf. cows	faecal samples + / tested	milk samples + / tested	Author
4	-	4/4	3/3	ALEXEJEV-GOLOFF 1935 (8)
34	-	-	2[1)]/34	DOYLE 1954 (9)
20	-	-	1/20	SMITH 1960 (10)
26	-	16/21	9/26	TAYLOR et al. 1981 (11)
-	86	22/86	9/77	SWEENEY et al. 1992 (7)
-	126	36/126	13[2)]/126	STREETER et al. 1995 (12)
22	-	-	3[3)]/22	CHANG et al. 1996 (13)
2	4	-	3[4)]/6	MILLAR et al. 1996 (14)
4	131	10/119	4[5)]/135	HAMMER 1999 (15)
-	-	-	4[6)]/201	ACMSF 2000 (16)

[1)] udder tissue [2)] 10 colostrum, 3 milk [3)] PCR only from macrophages [4)] PCR only [5)] clinically diseased cows only [6)] bulk milk, dairy level

3.2 Prevalence in heat treated milk and milk products

About the prevalence in heat treated milk and products thereof some data are available. Recent reports with special relationship to practice show that *M. paratuberculosis* can be present in commercial dairy products (Table 2). Reported results obtained by PCR and related techniques often show a much higher presence of *M. paratuberculosis* DNA in the samples, however, in the table only results after cultural confirmation are considered.

Tab. 2: Cultural detection of *M. paratuberculosis* in commercial dairy products

Product	processing conditions	samples total/***positive***	Author
whole milk	min. 71.7 °C for 15 s	244/***4***	AYELE et al. 2005 (17)
whole milk	“pasteurized”, no details given	702/***20***	ELLINGSON et al. 2005 (18)
whole milk	72-74 °C for 15-28 s	228/***3***	GRANT et al. 2002 (19)
semi skim milk	72-75 °C for 14-25 s	179/***5***	GRANT et al. 2002 (19)
skim milk	72 °C for 15-17 s	160/***2***	GRANT et al. 2002 (19)
whole and skim milk	“HTST”, no details given	124/***2***	HASSAN et al. 2005 (20)
milk	“pasteurized”, no details given	18/***1***	PAOLICCI et al. 2005 (21)
milk	138 °C for 30 s	30/***1***	PAOLICCI et al. 2005 (21)
soft cheese*)	feta cheese, no details given	42/***1***	GAZOULI et al. 2003 (22)
powdered infant milk	no information**)	51/***1***	HRUSKA et al. 2005 (23)

*) no information given, whether processed from raw or heat-treated milk
**) it should be noted that milk powder for this type of product is made from HTST-treated milk, and has undergone subsequent further heat treatments during evaporation and spray drying comprising an estimated log reduction of *M. paratuberculosis* of 10-14 $\log_{10}$ cycles

Based on the results of heating experiments with a commercial scale pasteurizer the survival of *M. paratuberculosis* can indeed be expected (24). Unfortunately only qualitative data were generated during these experiments, whereas for utilization in exposure assessment quantitative data are required.

Within the normal measuring range, the bacterial kill under conditions of heating is based on a linear function, i.e. the bacterial count becomes uniformly reduced as a function of temperature and holding time down to a point at which surviving organisms are no longer detected. Although during heating, there is a quite substantial reduction of the initial *M. paratuberculosis* count by more than 5 logs, low numbers of surviving bacteria may still be detected for a fairly long period, even at temperatures up to 90 °C at a holding time of 60 s (25). A 7 log reduction was achieved in whole milk, skim milk and cream at heating conditions in the UHT range (2-5 s at 135 °C), however, low numbers of survivors still remained detectable (26).

Currently there are only very few reports in the literature dealing with the detection of *M. paratuberculosis* in milk products (Table 2). However, some data on possible survival in soft, semi hard and hard cheese during manufacture under laboratory conditions are published.

On the survival of *M. paratuberculosis* in soft cheese (Hispanic style) data are published by SUNG and COLLINS (27). In cheese made from milk spiked with non-heated *M. paratuberculosis* at a level of 10^4 cfu/ml a decimal reduction time of 59.9 days was estimated. Using sub lethally injured cells (62 °C for 240 sec) the decline was faster resulting in an estimated D-value of 36.5 days.

SPAHR and SCHAFROTH (28) used raw milk spiked at a level of 10^4-10^5 cfu/ml (declumped cells) to manufacture hard cheese (Swiss Emmentaler) and semi hard cheese (Swiss Tilsiter). Calculated D-values for the hard cheese were 27.8 days, for the semi hard cheese 45.5 days. After 120 days of ripening *M. paratuberculosis* at low levels was still detected. 3-4 log were estimated as possible reduction during ripening.

DONAGHY et al. (29) determined D-values of 90, 96 and 107 days during manufacture of cheddar using three different strains of *M. paratuberculosis*.

3.3 Prevalence in other foods and the environment

As reported for *M. avium* (30), besides milk other foods may be contaminated by *M. paratuberculosis*. Slaughtering of subclinically infected animals may lead to a contamination of the carcass if the gut is accidentally cut during evisceration. Additionally lymph nodes and other tissue may be contaminated by bacteraemia. Few data on the prevalence in meat and none for meat products are published. Studies on thin cows at slaughter in the USA and Switzerland showed strong evidence that meat could be contaminated. In the US study *M. paratuberculosis* was detected in 11.1 % of 189 dairy cows and in 0.7 % of 350 beef cattle by culture in lymph nodes associated to meat *(Ln cervicalis superficialis* and *Ln popliteus)* (31). In the Swiss study diaphragm muscle of 14 cows that were positive by culture in ileocaecal lymph nodes was tested by realtime PCR. Ten of these were positive by PCR, however, culture was not done with the muscle (32). During own investigations on 42 samples of ground beef from a region with endemic paratuberculosis in Germany no *M. paratuberculosis* was detected. *E. coli* was detected in 41 of these samples in colony counts up to 10^3 cfu/g, so considerable faecal contamination could be supposed.

For the prevalence of *M. paratuberculosis* in vegetables and lettuce presently no data are published. A contamination by on plant fertilization would be possible if manure from diseased is used. Respective laboratory trials have been performed in the Czech Republic (33). Cultivation of lettuce, radish and tomatoes for 4 weeks in contaminated soil showed that besides surface contamination there was an uptake of *M. paratuberculosis* into leaves, stem and fruits.

For other mycobacteria water is known as a vehicle for transmission. Due to its high tenacity to environmental influences (34, 35) *M. paratuberculosis* may survive for months or even years in water, soil and untreated manure (36, 37), so recontamination of food from these sources must also be considered. The presence of *M. paratuberculosis* in the watertreatment chain for domestic use and in surface water was shown by PICKUP et al. (38, 39).

Natural reservoirs as, e.g. wild rabbits (40) also may contribute to a contamination of the environment and to subsequent infection of cattle or recontamination of food, particularly of vegetables.

3.4 Scenarios to predict the range of possible exposure through milk

As a scenario to predict the range of possible exposure a worst case scenario (dilution model) was applied based on rather conservative assumptions regarding the possible introduction of *M. paratuberculosis* originating from a herd with diseased animals into milk supplied to a dairy. The parameters were a small herd of 15 animals with a low milk yield of 10 l per animal and milking, a small road tanker of 10,000 l, and a small dairy storage tank of 50,000 l. For direct contamination the data of SWEENEY et al. (7) of 2-8 cfu/50ml, and for faecal contamination 1g per cow and milking with a content of 10^8 cfu/g were applied.

Assuming a direct secretion of the organism with the milk from a single cow or all cows, calculation would result in an expected contamination at the dairy level of 0.16 or 2.4 cfu/l of raw milk. When referred to a contamination of milk by faeces at the dairy level, the same scenario would result in 8,000 cfu/l for a single cow being a carrier or 120,000 cfu/l for all cows. It should be noted that these estimates are based on a worst case assumption, i.e. a small herd with a low milk production and a heavy faecal contamination (1 g/l) of the milk. In practice, dilution effects will be higher. Additionally, it should also be taken into account that an effect of heating will obviously occur, thus causing a more than 100,000-fold reduction of the bacterial count. Taking the highest calculated initial count, the expected level after heating will be about 1 cfu/l of milk.

Another, broader approach to estimate the population exposure via pasteurized milk for human consumption in The Netherlands was published by NAUTA and van der GIESSEN (41):

In the event of a direct shedding of *M. paratuberculosis* into milk, subclinically diseased animals will contribute with approx. 2-8 cfu/50 ml (7). Exact data for clinically diseased animals are not known. Estimates assume levels of up to 10^4 cfu/l. In the event of faecal contamination of milk, estimates are based on an introduction of 10^0 - 10^3 cfu/g of faeces by subclinically diseased animals and of 10^2 - 10^9 cfu/g of faeces by clinically diseased animals.

Faecal contamination of milk is assumed to be 10 mg/l. Furthermore, a herd prevalence of approx. 20 % has to be taken into account for The Netherlands. Further assumptions for calculation were a herd size of 100 animals with a share of clinically diseased animals

of 5 - 10 % (worst case), and a 100-fold reduction of the initial count by heating. The final result was an estimated contamination of approx. 0.5 cfu for each litre of marketed pasteurized milk.

Since clinically diseased animals contribute with 99 % to such a contamination, a stringent exclusion of such animals from milk production would reduce the mean exposure to 0.06 cfu/l, which means 6 out of 100 packages of 1 l contaminated with 1 cfu/l. Taking also into account a reduction of the initial count by more than 10^5 times instead of a mere 100 times due to heating, this would reduce the contamination rate to 5 milk packs among 10,000 packs.

Not jet considered in both approaches are the conditions prevailing in practice where the process steps before filling (filtration and purification of the milk in the separator etc.) lead to a further reduction of counts. It is a decisive advantage of all these scenarios that *M. paratuberculosis* is incapable of multiplication outside the host's body. Thus, its elimination or reduction within the food chain may be regarded in a similar way as, e.g. the situation for chemical residues.

The consumption of raw milk, particularly from small scale supplies could lead to much higher exposures because there are almost no factors of reduction like dilution and heat treatment.

3.5 Human exposure (epidemiological data)

Non-dietary exposure:

Not many data are available on a real exposure of the population to *M. paratuberculosis*. Crohn's disease is occurring in all groups of the population, a significant accumulation in groups which might more likely be in contact with the organism as, e.g. farmers or veterinarians has not been observed until now. A higher exposure of the rural population, however, can be estimated according to data from CHERNEY and COLLINS (42). These authors recorded in serum samples from two groups of healthy blood donors (300 from a rural, 200 from an urban population) significantly higher antibody titres against *M. paratuberculosis* in the rural group.

Another hint on regional exposure is reported by HARRIS and LAMMERDING (43). In their review they mention observations that people who have immigrated from regions or countries with low disease prevalence to regions with high disease prevalence acquire the same disease prevalence as the local non-immigrant population. However, there is not even a suggestion on a possible source for this exposure.

Dietary exposure:

In general an exposure via multiple pathways is likely (Figure 2). The highest input into the food chain will be caused by diseased cattle due to the large amounts of faeces produced and the very high colony counts of *M. paratuberculosis* that may be contained (10^8-10^9 cfu/g). As summarized before, a dietary exposure of humans is possible via raw and heat treated milk, and respective products. No real data about quantities of ingested *M. paratuberculosis* are available. Applied scenarios and interpretation of experimental data lead to an estimate of low or even very low numbers. For meat and related products, vegetables and potable water not even an assumption is possible due to missing data.

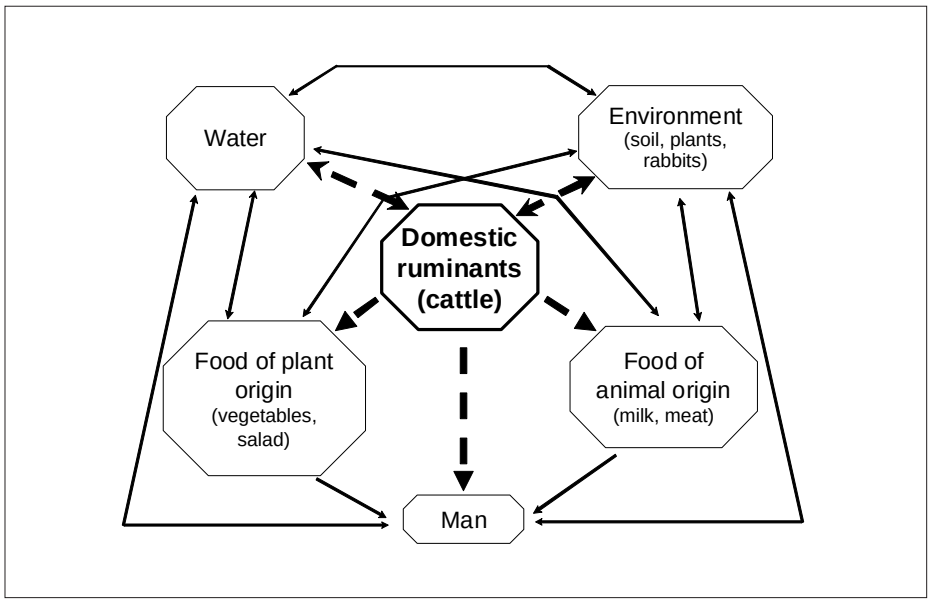

Fig. 2: Pathways for the spread of *M. paratuberculosis* in food and environment

4. Hazard characterization

Hazard characterization is a qualitative or quantitative description of the severity and duration of adverse effects that may occur in a host after ingestion of a microorganism in food. The ideal outcome is an establishment of a clear dose-response relationship after a dose-response assessment (1).

With regard to *M. paratuberculosis* this target cannot currently be met. More information on the possible relation of *M. paratuberculosis* to the host is needed to complete the hazard characterization, e.g. individual host susceptibility characteristics as age, health, medication, psychological status, immune status, dietary incompatibilities and genetic factors. Recent reviews of the issue (44, 45, 46) show that there are more open questions than solutions and the discussion on the pathogenic potential of the organism is still ongoing. Though this discussion is not subject of this article an open question with regard to exposure assessment should be mentioned:

In the understanding of Crohn's disease the disease is in the beginning characterized by a breakdown of the physiological barrier in the gut. The result is an inflammation complex that is self-maintaining due to many reasons. One identified reason is bacterial products penetrating the broken barrier. Whether *M. paratuberculosis* is causing this breakdown or is as a bacterial product one of the triggers of the perpetuating inflammation is not known. It must be considered, however that in the last case even low doses may then cause a severe effect. With regard to the high immunological efficacy of mycobacterial antigens, which, e.g. is utilized in the complete Freund's adjuvant, even killed *M. paratuberculosis* cells– and other mycobacteria – may be of concern. Important might be whether heat injured *M. paratuberculosis*, present in pasteurized milk, are still infectious. During development of pasteurization equipment and definition of heating parameters in Germany testing for the inactivation of *M. tuberculosis* or *M. bovis* was mandatory. These

tests were performed by parenteral application of heated milk or centrifugates thereof into Guinea pigs which still is the most sensitive animal model for this purpose. Later also culture methods were applied in parallel sometimes showing positive results although the animal experiment was negative (47). That could be an indication that the infectiosity was destroyed by the heat treatment whereas cultivability was still given. It could be at least assumed that something similar would be possible for *M. paratuberculosis* which would cast a different light onto exposure via pasteurized milk.

5. Risk characterization/consideration

Risk characterization should integrate the three steps hazard identification (HI), exposure assessment (EA) and hazard characterization (HC) to obtain a risk estimate. This estimate should preferably be a quantitative estimate of the likelihood and severity of the adverse effects that could occur in a given population. According to the data available, particularly considering missing information and uncertainty, only a qualitative estimate of risk may be obtained (1).

Summarizing briefly the data presented here will show that on the basis of present knowledge a qualitative risk estimate can be obtained at best:

HI *M. paratuberculosis* must be regarded as a hazard due to a precautionary approach. With emphasis on new knowledge that has regularly to be re-evaluated

EA Very few data are available. The applied scenarios predict a possible but low contamination of pasteurized milk and of milk products; more quantitative data on contamination rate of milk and other food are needed. The consumption of raw milk and respective products, particularly from small-scale marketing may lead to enhanced exposure. Studies on thermal tolerance indicate that a small number of cells will survive high temperature short time treatment (HTST) of milk. However, as far as no minimum infective dose is known the impact on human health cannot be judged.

HC *M. paratuberculosis* might be an issue for a group of Crohn's disease patients. The database to prove or disprove an association between the organism and Crohn's disease, including a clear dose response relationship is insufficient. The elaboration of a sufficient database is not expected within the coming years (3). Though the report to the European Commission stating this was issued 2000 this situation has not changed.

Focusing on pasteurized milk and milk products made from pasteurized milk the risk for consumers to acquire Crohn's disease is probably very low. This is just a qualitative estimate drawn from a weak database, and is to be re-evaluated as soon as new data are available. According to the "milk and water study" milk, milk products and water are of no influence in the aetiology of Crohn's disease (48).

6. Risk management options

As far as risk management options are considered on the basis of this risk estimate two important questions should be answered:

1. Is the risk tolerable until new data may lead to another risk characterization?
2. Are measures for the reduction of *M. paratuberculosis* necessary and economically justified considering the possibly low risk?

The occurrence of *M. paratuberculosis* in milk and the resulting estimates of human exposure through raw and HTST treated milk will become important as soon as risk characterization confirms an association between the organism and Crohn's disease. Until such date, the estimates have to be considered as measures taken under the precautionary principle. The question is, should action be taken to reduce the exposure to *M. paratuberculosis* even though the causal link is not established? If action should be taken are there risk management options that will lead to a reduction of the organism in milk and a subsequent reduction of risk?

Risk management in the framework of risk analysis of the Codex Alimentarius would lead to e.g. governmental action making measures as listed below mandatory (1).

6.1 On-farm control

There is common agreement, that on-farm control is the best measure to reduce the introduction of *M. paratuberculosis* in the food chain (49). The input in milk is merely due to clinically diseased animals and to subclinically diseased animals short before clinical symptoms occur. Excluding these animals from milking in a short term view will lead to a considerable reduction of the organism in milk. According to the EU hygiene legislation milk of diseased animals must not be used for human consumption. This will lead to an exclusion of the clinical diseased animals if obeyed. Implementation of disease control systems will in a mid- to long-term view lead to a further reduction because – even if tests to detect subclinically diseased animals are not that convincing – animals in a late stage of subclinics should be identified and thus be subsequently excluded from milking. With regard to these issues management options for a reduction of the input of *M. paratuberculosis* are the improvement of the legal demand to exclude clinical diseased animals from milking and the implementation of economically or legally enforced disease control programmes. The second option of course needs considerable funding.

6.2 Processing options

Thermal tolerance data indicate that *M. paratuberculosis* is more thermoresistant than many vegetative bacteria. However, during HTST treatment even at the lowest legally defined conditions (15 s, 72°C), a 5 log reduction is achieved though some survival might occur (reviewed by 44). Further reduction might be possible by application of other processing options as homogenization, centrifugation and filtration (50, 51). Until the impact of low numbers of the organism in milk on human health is uncertain precautionary measures should be applied. On the other hand changes in heating conditions to higher temperatures and extended holding times are almost of no further effect, which would not justify recommendations for changes of heating conditions. Data on effects of other processing options must be elaborated first until recommendations can be deducted.

6.3 Recommendations for consumption

Due to the statement of the expert consultation at the German Federal Institute for Health Protection of Consumers and Veterinary Medicine (5) recommendations to avoid consumption of milk and milk products to prevent Crohn's disease are not justified based on the available data.

With respect to a possible higher exposure due to raw milk and respective products, however, it is recommendable at least for risk groups (Crohn's disease patients, patients with other bowel diseases, immune suppressed persons) to avoid consumption of these products.

7. Conclusions

To conclude it can be summarized, that there is no sufficient database for a formal quantitative risk assessment. Even a qualitative risk assessment is hardly possible due to missing data. As far as estimable a risk for the population to acquire Crohn's disease via milk or milk products seems to be low. Nevertheless, the still existing uncertainty demands the application of precautionary measures. As a risk management option on-farm control of paratuberculosis in a mid- or long-term view will lead to a considerable reduction of the input of *M. paratuberculosis* into the food chain. By means of short-term risk management for milk exclusion of clinically diseased cows from milking and processing options as heat treatment and additional processing options may be valuable. This needs to be further evaluated on a scientific basis.

Recommendations on restricted consumption of milk and milk products seem not to be justified, except for persons at higher risk to avoid the consumption of raw milk and respective products.

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9. Summary

Hammer, P.: *Mycobacterium avium ssp. paratuberculosis* in milk: risk considerations. Kieler Milchwirtschaftliche Forschungsberichte **59** (4) 209-225 (2007)

06 Veterinary medicine and hygiene (mycobacterium paratuberculosis, milk, risk consideration, exposure, Crohn's disease)

Information on the importance of *Mycobacterium avium ssp. paratuberculosis* (*M. paratuberculosis*) for animal health, consumer health, and for processing including heat resistance can be used for a risk assessment within the Codex Alimentarius approach on microbiological risk analysis. Although a formal risk assessment according to the Codex procedure is not yet feasible for *M. paratuberculosis* the structure of the procedure can be followed. A risk assessment is a four step procedure consisting of i) hazard identification, ii) exposure assessment, iii) hazard characterization and iiii) risk characterization.

Hazard identification is a qualitative process aiming at the identification of microorganisms of concern and the evaluation whether they represent a potential hazard when present in food. For the time being it cannot be excluded that *M. paratuberculosis* may adversely affect human health because there is still lack of evidence when it could be at least one factor in Crohn's disease. As long as there is uncertainty precautionary measures should be applied and *M. paratuberculosis* be regarded as a hazard.

Exposure assessment preferably should result in a quantitative estimate of level and likelihood of the occurrence of a pathogen in a certain food. The prevalence of *M. paratuberculosis* in raw milk is mainly influenced by the health status of the cow including endogenous spread of the organism but also faecal contamination during milking. About the prevalence in heat treated milk some data are available. Heating experiments show a quite substantial reduction of the initial count by more than 5 log cycles; merely, small numbers of surviving bacteria are detected occasionally. Scenarios to predict the occurrence of *M. paratuberculosis* in heat treated milk result in a calculated exposure down to 0.0005 cfu/l corresponding to 5 milk packs contaminated with 1 cfu each among 10 000 1 l packs.

Hazard characterization is a qualitative or quantitative description of the severity and duration of adverse effects that may occur in a host. The ideal outcome of this step is an establishment of a dose-response relationship . For *M. paratuberculosis* the knowledge is presently insufficient.

In terms of risk characterization there is no sufficient database for a formal quantitative risk assessment. Even a qualitative risk assessment is hardly possible due to missing data. As far as estimable a risk for the population to acquire Crohn's disease via milk or milk products seems to be low. Nevertheless, the still existing uncertainty demands precautionary measures. As a risk management option on-farm control of paratuberculosis

in a mid- or long-term view will lead to a considerable reduction of the entry of the organism into the food chain. Short term risk management options are heat treatment and additional processing measures.

Zusammenfassung

Hammer, P.: *Mycobacterium avium ssp. paratuberculosis* in Milch: Eine Risikoerörterung. Kieler Milchwirtschaftliche Forschungsberichte **59** (4) 209-225 (2007)

06 Veterinärmedizin und Hygiene (Mycobacterium paratuberculosis, Milch, Risikoerörterung, Exposition, Crohnsche Erkrankung)

Informationen zur Bedeutung von *Mycobacterium avium ssp. paratuberculosis* (*M. paratuberculosis*) für die Tiergesundheit und die menschliche Gesundheit sowie technologische Gesichtspunkte, eingeschlossen Fragen der Hitzeresistenz, können für eine Risikoerörterung im Rahmen der im Codex Alimentarius entwickelten mikrobiologischen Risikoanalyse verwendet werden. Obwohl eine formale Risikobewertung im Sinne des Codex für *M. paratuberculosis* derzeit noch nicht durchgeführt werden kann, ist die dort vorgegebene Struktur für eine Erörterung des möglichen Risikos geeignet. Eine Risikobewertung sollte aus den vier Schritten Gefahrenidentifizierung, Expositionsabschätzung, Gefahrencharakterisierung und Risikocharakterisierung bestehen.

Die Gefahrenidentifizierung ist ein qualitativer Prozess, der zur Identifizierung von Mikroorganismen und ihres möglichen Gefährdungspotentials für die menschliche Gesundheit bei Anwesenheit in einem Lebensmittel führen soll. Derzeit kann nicht ausgeschlossen werden, dass *M. paratuberculosis* eine solche Gefahr darstellt, da immer noch offen ist, ob und welche Rolle der Keim beim Morbus Crohn spielt. Solange diese Unsicherheit besteht, sollte das Vorsorgeprinzip beachtet und *M. paratuberculosis* als entsprechende Gefahr betrachtet werden.

Die Expositionsabschätzung soll, vorzugsweise quantitativ, die Menge und die Wahrscheinlichkeit mit der ein pathogener Keim in einem bestimmten Lebensmittel vorkommen könnte angeben. Das Vorkommen von *M. paratuberculosis* in Rohmilch wird dabei hauptsächlich vom Gesundheitszustand der Kuh und der dadurch bedingten endogenen Kontamination der Milch und der fäkalen Verunreinigung der Milch während des Melkens beeinflusst. Zum Vorkommen in erhitzter Handelsmilch liegen inzwischen einige Daten vor. Erhitzungsversuche führen zu einer deutlichen Reduzierung der Ausgangskeimzahl um mehr als 5 log-Stufen, eine völlige Abtötung gelingt jedoch nicht. Modelllrechnungen zum Vorkommen von *M. paratuberculosis* in erhitzter Milch ergeben Schätzwerte bis hinunter zu 0.0005 cfu/l, entsprechend 5 mit je 1 cfu kontaminierter Milchpackungen aus 10.000 Packungen a 1 l.

Die Gefahrencharakterisierung ist eine qualitative oder quantitative Beschreibung von Schwere und Dauer möglicher negativer Einflüsse durch einen Mikroorganismus in einem Wirt. Idealerweise kann hierbei eine klare Dosis-Wirkungsbeziehung ermittelt werden. In Bezug auf *M. paratuberculosis* reicht das heutige Wissen aber hierfür nicht aus.

Eine formale quantitative Risikobewertung kann auf der bestehenden Datengrundlage derzeit nicht durchgeführt werden. Selbst eine qualitative Bewertung ist auf dieser Basis nur eingeschränkt möglich. Soweit zu beurteilen, ist das Risiko der Bevölkerung durch den Verzehr von Milch- und Milchprodukten an Morbus Crohn zu erkranken, wahrscheinlich gering. Die bestehende Unsicherheit erfordert jedoch vorsorgliche Maßnahmen zur

Risikominimierung. Zur Reduzierung des Eintrags von *M. paratuberculosis* in die Nahrungskette sind mittel- bis langfristig Bekämpfungsprogramme auf Hofebene geeignet. Kurzfristig könnten neben der Erhitzung weitere technologische Verfahren geeignet sein.

Résumé

Hammer, P.: *Mycobacterium avium ssp. paratuberculosis* dans le lait: discussion sur les risques. Kieler Milchwirtschaftliche Forschungsberichte **59** (4) 209-225 (2007)

06 Médecine vétérinaire et hygiène (Mycobacterium paratuberculosis, lait, discussion sur les risques, exposition, maladie de Crohn)

Les informations sur l'importance *des Mycobacterium avium ssp. paratuberculosis* (*M. paratuberculosis*) pour la santé animale et humaine ainsi que les aspects technologiques, les questions sur la résistance à la chaleur incluses, peuvent être utiles dans la discussion menée dans le cadre du Codex Alimentarius sur les risques microbiologiques. Bien qu'une évaluation formelle des risques dans le sens du Codex ne soit actuellement pas encore réalisable pour *M.* paratuberculosis, la structure établie facilite une discussion sur les risques potentiels. Une évaluation des risques devrait comprendre les quatre paramètres suivants : identification du danger, estimation sur l'exposition, caractérisation du danger et caractérisation des risques.

L'identification du danger est un processus qualitatif qui doit conduire à l'identification des microorganismes et de leur potentiel de risque pour la santé humaine en cas de présence dans des produits alimentaires. Actuellement, on ne peut pas exclure que *M. paratuberculosis* représente un tel danger, puisqu'il n'est pas encore clarifié, si et quel rôle le pathogène joue dans la maladie de Crohn. Tant que cette insécurité existe, le principe de précaution devrait être suivi et *M. paratuberculosis* considéré comme danger.

L'estimation d'exposition, de préférence quantitative, devrait indiquer la quantité et la probabilité avec laquelle un pathogène pourrait être présent dans un certain produit alimentaire. La présence de *M. paratuberculosis* dans le lait cru est influencée principalement par l'état de santé de la vache, la contamination endogène du lait et de la pollution fécale du lait pendant la traite. Entre-temps quelques données sont disponibles sur la présence du pathogène dans le lait commercial chauffé, Des essais d'échauffement mènent à une réduction sensible de la charge bactérienne initiale de plus de 5 cycles log, mais une élimination complète n'est pas encore possible. Des calculs modèles sur la présence de *M. paratuberculosis* dans du lait chauffé fournissent des valeurs estimatives allant aussi bas que 0.0005 ufc/l, correspondant à 5 emballages de lait contaminé avec chacun 1 ufc sur un ensemble de 10.000 emballages à 1 l.

La caractérisation du danger est une description qualitative ou quantitative portant sur la gravité et la durée d'effets négatifs possibles provoqués par un microorganisme dans l'hôte. Au cas Idéal, une corrélation claire entre dose et effet peut être déterminée. En ce qui concerne *M. paratuberculosis,* les connaissances actuelles sur ce sujet sont insuffisantes.

Sur la base existante des données, il n'est actuellement pas possible de faire une évaluation quantitative formelle des risques. De même une évaluation qualitative sur cette base n'est possible que de façon restrictive. Au niveau des connaissances

actuelles, le risque que la population de tomber malade de Morbus Crohn à cause de la consommation de produits laitiers est probablement faible. L'insécurité existante exige toutefois des mesures prévoyantes concernant la minimisation du risque. Pour réduire l'entrée de *M. paratuberculosis* dans la chaîne alimentaire, des programmes de lutte au niveau de la ferme sont appropriés à moyen et à long terme. À court terme, d'autres procédures technologiques, à part l'échauffement, pourraient être utiles.