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FOR DEBATE
Coxiella burnetii and milk pasteurization: an early application of the precautionary principle?

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SUMMARY

Stringency of milk pasteurization has been established on requirements for *Coxiella burnetii* as being the most heat-resistant organisms of public heath significance. This paper discusses the estimation of the efficiency of pasteurization time/temperature combinations as required in regulations for food safety. Epidemiological studies have been interpreted as *C. burnetii* being a significant pathogen causing clinical disease through ingestion of milk. The paper examines the evidence and challenges the designation of *C. burnetii* as a foodborne pathogen. Consequently it questions the need for pasteurization parameters to be established on its heat resistance characteristics.

INTRODUCTION

Milk pasteurization was introduced to prevent the oral transmission of tuberculosis, brucellosis, and other milk-borne infectious diseases. Early in the twentieth century, it was established that the cells of the tubercle bacillus were the most heat-resistant vegetative bacterial cells in milk. Therefore, the first recommendations for time and temperature combinations for pasteurization were established on this basis. However, pasteurization of milk is defined by the Codex alimentarius Committee for Food Hygiene [1] as 'a microbiocidal heat treatment aimed at reducing the number of any pathogenic micro-organisms in milk and liquid milk products, if present, to a level at which they do not constitute a significant health hazard. Pasteurization conditions are designed to effectively destroy the organisms *Mycobacterium tuberculosis* and *Coxiella burnetii*'. Thus the international definition points to the need for the destruction of *Coxiella burnetii* to protect the health of milk consumers.

C. burnetii is the cause of Q fever, recognized in 1935 as an occupational disease of workers in abattoirs in Australia and as a tick-transmitted disease in the United States [2]. After the Second World War, a high prevalence of Q fever and serological conversion was observed among the population in Europe and North America, in regions where raw milk and raw milk products were commonly consumed [3, 4]. There was a consensus that milk should not be consumed raw and, therefore, milk pasteurization was recommended. Studies were conducted in several countries to check the efficiency of heat against *C. burnetii* [3, 5–9]. Eventually time-temperature conditions for pasteurization published by US researchers in 1957 [10–12] became the international standard.

In the first part of this paper, we will indicate how these researchers used a safety factor, and will show that the recommended heating treatment not only provides at least 4·7 decimal reductions or 'log kills'

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Table. *Number of decimal reductions* (*log kills*) *of* C. burnetii *demonstrated experimentally, and values calculated for internationally recommended pasteurization time/temperature combinations, assuming a linear survival curve. Calculations were done with* $z = 4{\cdot}34\ ^{\circ}C$

Temp. (F)	Temp. (°C)	Decimal reduction time, *D*	Min. time of destruction plus 2 S.D.*	Corresponding number of decimal reductions	Combinations recommended by the authors	Corresponding number of decimal reductions	Presently recommended combinations	Corresponding number of decimal reductions
145	62·8	4·14 min	25·42 min	6·1	30 min	7·2		
	63	3·72 min					30 min	8·1
161	71·7	2·21 s	15·4 s	6·9	15 s	6·8		
	72	1·88 s					15 s	7·9

* S.D., Standard deviation.

(rather than 5 as usually reported), but plausibly even more. In the second part we will question if Q fever is a foodborne disease and if pasteurization is scientifically justified for the prevention of Q fever.

Heat resistance of *C. burnetii*

A number of studies conducted to measure the heat resistance of *C. burnetii* did not lead to any convincing conclusion related to the efficacy of time-temperature combinations used in pasteurizers [3, 5–9]. Enright *et al.* [11, 12] put an end to this by publishing undisputed results validated through infection studies in guinea pigs by intraperitoneal inoculation. Since the appearance of specific complement-fixing antibody was significantly induced by killed *C. burnetii*, the authors demonstrated the presence of infective viable microbial cells by two consecutive passages on guinea pigs. They used whole raw milk from an experimentally infected cow containing 10^5 infecting doses in 2 ml (5×10^4 infective doses/ml) and heated in the laboratory at temperatures from 60·6 to 66·1 °C for different lengths of time.

For the shortest heating times, viable cells were still present. For the longest heating times, no viable cells could be found. Linear regressions of $\log_{10}$(time) against temperature were calculated to determine two lines:

- the line A below which vials were still positive (containing at least one surviving cell);
- the line B over which no vial contained survivors (corresponding to the 'minimum time of destruction' according to the authors).

Positive as well as negative vials could be found between lines A and B.

A second series of experiments conducted by a regular commercial pasteurization plant from 68·1 to 72·8 °C confirmed the validity of the first series.

The authors based their recommendations for pasteurization conditions by adding two standard deviations or 97·7% confidence interval to the minimum times of destruction estimated by the regression B. They finally recommended two time-temperature combinations that have subsequently been universally recognized: 30 min at 62·8 °C (145 F) or 15 s at 71·7 °C (161 F).

The influence of temperature is, therefore, given by $z = 4{\cdot}34$ °C. These recommendations were then simplified as follows [1, 13]: 30 min at 63 °C or 15 s at 72 °C, thus providing an extra safety margin. Assuming the survival curves are straight lines, this would achieve eight decimal reductions.

If, for a given temperature $\log_{10}(a)$ is the ordinate of line A, and $\log_{10}(b)$ the ordinate of line B, then the most probable time t for which there is one survivor per vial is [14]:

$$\log_{10} t = 0{\cdot}63\ (\log_{10} b - \log_{10} a) + \log_{10} a$$

and the decimal reduction time is calculated with [14]:

$$D = t/\log_{10}(N),$$

where N is the initial number of microbial cells per vial.

The experimental data of Enright *et al.* [11] are reported in the Table together with calculated D values and numbers of decimal reductions corresponding to recommended treatments.

The experimental work of Enright *et al.* [11, 12] was performed carefully. It was the first study regarding *C. burnetii* where the results were modelled using statistical regression, and where a safety margin was

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used. However, the paper was not clear as to the origin of the *C. burnetii* cells subjected to heating: whether they were from one or several animals; and whether a single strain or a mixture of strains was used? The shape of survival curves was not studied, and it was not checked if the curve was linear or biphasic, i.e. having a second part or 'tail' indicative of a slower killing rate; therefore, the addition of two standard deviations by Enright *et al.* [11] did not guarantee a larger killing effect. While there is no certainty about the actual number of decimal reductions, one can nevertheless reasonably assume that, for the studied strain(s), pasteurization achieved between 4·7 [i.e. log $\log_{10}(5 \times 10^4)$] and 8 decimal reductions of *C. burnetii*.

Transmission of Q fever to people

It is well documented that *C. burnetii* is transmitted to man from infected wild or domesticated mammals, including farm animals and pets, by inhalation and by bites of haematophagous arthropods. The disease affects mostly farmers, veterinarians, researchers, abattoir workers and persons exposed to aerosols in dwellings situated down wind, or being in the vicinity of infected herds [15–49]. All outbreaks and sporadic cases reported for the last 50 years in Australia, France, Germany, Italy, and the United States were attributed to inhalation and sometimes to arthropod bites [23, 24, 26, 27, 31, 34, 36, 39, 47, 50–55]. No information is given of the infective dose.

In his comprehensive review, Wegener [3] noted the widespread opinion at that time: 'Milk is the most significant source among products of animal origin. Personnel in dairies and their families with the greatest use of raw milk are heavily infected in the regions with Q fever problems in North America and Italy.' This opinion on foodborne transmission was based on a survey in the United States where 10·7% of people consuming raw milk had a positive serological test, compared to 0·7% among non-exposed people. Other authors used the same argument on the basis of observations in England [4, 17, 56] and in other countries [18, 19, 25, 57–60]. Nevertheless several reports mentioned the oral route as possible but infrequent, circumstantial, or needing a very high dose [15, 33, 44, 61–63]. According to Enright *et al.* [11], milk of naturally infected cows contained the following numbers of guinea pig infective doses (ID) per millilitre: 1 (5 animals), 10 (5 animals), 100 (5 animals) or 1000 (3 animals), while the milk of an experimentally infected cow contained 10 000 guinea pig ID/ml. These microbiological loads should be compared to those of inhaled air around infected animals or herds. However, we could not find any indication of these.

A few publications that reported a correct epidemiological approach did confirm that seroconversion indicated infection, but not the clinical disease. Fishbein *et al.* [18] reported a significant association between seropositivity and drinking non-pasteurized milk products whether people were in contact with goats or not, but the article did not provide information about clinical disease. Benson *et al.* [62] indicated that 35% of prisoners drinking infected milk had a positive serological test against 4% in a non-exposed control group; yet the authors emphasized that no manifestations of disease were recorded. Hatchette *et al.* studied an outbreak affecting goats in Newfoundland (Canada):

> Risk factors associated with human infection [based on people with serological conversion, but where infection was not confirmed and no indication was given in the paper about manifestation of disease] on univariate analysis included being a farmer, milking goats, assisting with kidding, handling placentas, shovelling manure, having direct contact with goats, eating cheese made from goat milk, petting goats, feeding goats, being a worker, smoking tobacco, and drinking alcohol. When only a multivariate analysis was used, the following were significant risk factors for infection with *C. burnetii*: contact with the placenta ($P < 0{\cdot}001$), smoking history ($P = 0{\cdot}001$), and eating cheese made from [pasteurized] goat milk ($P = 0{\cdot}022$). Consumption of goat milk itself was not associated with an increased risk of infection (OR 1·07) [30].

The authors concluded: 'The reason for the association between ingesting goat cheese and developing Q fever is not clear and suggests further study is needed. At present, this is an epidemiological association only, as *C. burnetii* has not been recovered from the goat cheese.'

There is also evidence from Australia that indicates direct contact (inhalation) with *C. burnetii* is more important in causing Q fever than other exposure including ingestion, as detected by immunological reactivity. Q fever has been a notifiable disease in Australia since 1977 with about 600 cases reported each year (range 202–870) [64, 65]. The majority of notified cases (60%) are from people employed in the meat industry as abattoir workers. About 30% of notified cases of Q fever are from the agricultural industry [64]. This would represent a Q fever

notification rate of 1240/100 000 and 164/100 000 for meat and agricultural sectors respectively. In contrast, immunological reactivity is more commonly found in the agricultural rather than the meat industry.

In Australia, immunological testing of people presenting for Q fever vaccination programmes for people at risk of infection in meat works or rural communities shows that prior to vaccination 17% of meat industry workers compared to 28% from the agricultural industries (including farm families) had positive reactions indicating previous exposure to *C. burnetii* [65]. All cows' milk sold in Australia must be pasteurized in accordance with Food Standards regulations and non-pasteurized milk is only available to farming families. It is also of interest to note that 85% of notified cases of Q fever in Australia are males and 70% of cases are between 20 and 50 years [65]. This pattern of disease is different from potential exposure through consumption of non-pasteurized milk.

Some authors accepting the foodborne transmission paradigm assumed that the form of the disease could be different according to the route of contamination: hepatitis for ingestion, pneumonia for inhalation [18, 28, 58, 66–70]. It is now recognized that this is not true [71].

CONCLUSION

From what is reported above, it seems more than plausible that clinical disease of Q fever results only from inhalation of *C. burnetii* and sometimes arthropods bites. Ingestion of *C. burnetii*-contaminated milk or milk products may result in serological conversion potentially indicating infection but not necessarily clinical disease. In addition it is likely that seroconversion follows the ingestion of inactivated cells as well as of live cells. Therefore, one may question:

(1) Should Q fever be still listed among the foodborne zoonoses?
(2) Should temperature and time conditions for milk pasteurization still be based on the heat resistance of *C. burnetii*?

If the answer is 'no' to both questions, the historical decision to pasteurize milk in order to kill *C. burnetii*, made almost 50 years ago, could be considered retrospectively as an early example of the application of the precautionary principle.

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DECLARATION OF INTEREST

None.

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