Inventarisation and management of the public health risk of Q fever (*Coxiella burnetii*) in the European Union

Internship at the Federation of Veterinarians of Europe

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Summary

Q fever is a zoonotic disease caused by the bacterium *Coxiella burnetii* and endemic in most parts of the world. Cattle, sheep and goats are the primary animal reservoirs but many other animals can become infected.

In the Netherlands, there has been a sudden increase in the number of human Q fever cases since the beginning of 2007. In 2007, 2008 and 2009 respectively there were 168, 1000 and more than 2300 cases. This instigated a large multidisciplinary research portfolio in the Netherlands. There has been discussion whether the number and severity of Q fever cases have been under-reported in the years before 2007. Recent results of a sero-prevalence study suggest that under-reporting has probably not been the case.

Because of the high numbers of *C.burnetii* bacteria shed after abortion, the high abortion rates and the fact abortion waves and human cases were found in the same area, dairy goat farms are believed to be the main source of the Q fever outbreaks in the Netherlands. It is hypothesized that the outbreak in the South of the Netherlands is typical for the Dutch farming situation: large dairy goat farms using deep litter systems in a densely populated area.

Measures taken by the Dutch government are aimed at the dairy goat and to a lesser extent the dairy sheep sector. Since 2008 the Dutch government took several measures with the most drastic actions at the end of 2009, when the decision was made to cull all pregnant and male animals on infected farms.

At this moment there doesn't seem to be a real problem with Q fever in other European countries to the same extent as in the Netherlands. There are however regions with a similar situation as in the Netherlands: large dairy goat farms situated in densely populated areas. For that reason it would be a good idea to monitor the situation closely.

One of the lessons learned is that it is essential that veterinarians, doctors, farmers, researchers and veterinary and public health institutes share information. Optimizing animal health and minimizing public health risks can only be assured by working together.

Introduction

In the past few years there has been a sharp increase in the number of reported human cases of Q fever in the Netherlands. Until 2007 there were only about twenty reports of human cases per year. In 2007 suddenly there were 168 cases, in 2008 1000 cases and in 2009 over 2300 cases in the Netherlands. This is the largest human outbreak of Q fever ever reported. Because the disease used to be relatively rare, the sharp increase in human Q fever cases instigated many new research projects in the Netherlands.

This unique situation in the Netherlands could provide new insights for the development of Q fever management for the rest of Europe. Questions that arise are:

- Is this Q fever outbreak typical for the Dutch farming situation?
- What kind of measures did the Dutch government take?
- What are the public health risks for Europe and how should it manage Q fever?

This report provides an up to date review of actual information about the disease and the estimated public health risks involved. Furthermore, it provides an identification of lacking information about the disease and epidemiology and it describes the current policy of the Dutch government and its potential shortcomings.
In addition, it is important to assess the public health risk for the Netherlands, as well as for the European Union. There is a need to estimate the risk of spread to other European countries. Moreover, it needs to be determined whether and in what form a disease control plan is needed for Europe.

Methods

There are six possible programmes to follow during the last year of Veterinary Medicine at the Utrecht University in the Netherlands: Small Animal Medicine (e.g. dogs, cats), Large Animal Medicine (cattle, pigs, poultry), Equine Medicine, Veterinary Public Health, Veterinary Science and Management & Policy. The Management & Policy programme consists of ten weeks of education about the food chains of cattle, pigs and poultry, a minor in the field of management and policy and two internships (six weeks and twelve weeks).

This report is written by a Veterinary Medicine student of the Utrecht University in the Netherlands in her last year in the Management & Policy programme. The report was made during a three-month internship at the Federation of Veterinarians of Europe (FVE) in Brussels (Belgium).

Sources for this report were scientific reports, announcements of official organisations, interviews with experts and reports in the media. The interviews took place by telephone or in a personal setting.

Facts

Background information on Q fever

The bacterium

Figure 1: The bacterium Coxiella burnetii

Q fever is a disease caused by the bacterium *Coxiella burnetii,* an aerobic Gram-negative highly resistant bacterium. Cattle, sheep and goats are the primary animal reservoirs but many other animals like pets, rodents and birds can become infected. Q fever is a zoonotic disease, which means that it can be transmitted from animals to humans.

The disease in humans and animals

Humans

Most cases of Q fever in humans are reported to be asymptomatic (60%) or associated with mild flu-like symptoms. In more severe cases disease usually begins with acute severe headache and high fever. Other symptoms that could be seen are dyspnoea, endocarditis and possibly complications during pregnancy. Pneumonia is the predominant clinical presentation of the current Q fever cases in the Netherlands. The incubation time of the disease is two to six weeks.

Animals

As in humans, most infections in animals are asymptomatic. In cattle an infection is usually asymptomatic, but may result in abortion, subfertility and metritis (Arricau-Bouvery and Rodolakis, 2005). In small ruminants Q fever can cause abortion, stillbirth, retention of foetal membranes, endometritis and infertility. Abortion usually takes place towards the end of pregnancy (Arricau-Bouvery and Rodolakis, 2005; Muskens et al., 2007; Wouda and Dercksen, 2007). In most cases the affected animal doesn't show any clinical signs prior to abortion, but in a minor number of cases the animal is slow and has a reduced appetite (Wouda and Dercksen, 2007; Arricau-Bouvery and Rodolakis, 2005; Van den Brom and Vellema, 2009).

Mode of spreading of the disease

Urine, faeces, placentas, membranes and amniotic fluid of infected animals can be infectious. However, shedding of bacteria is highest during abortion or birth. An infected placenta contains between 100 million and one billion bacteria per gram (public statements by P. Vellema, 2009).

The disease can be spread to human via infected ticks, via aerosols, via the gastrointestinal tract (raw dairy products) and through blood transfusions. Infection via aerosols is the most common form for humans to become infected (Marrie, 1990). The National Institute for Public Health and the Environment (RIVM) considers the inhalation of contaminated dust to be the main source of infections of humans. Transmission between humans has been only incidentally described (Mann et al., 1986).

The bacterium can survive for months to years in the environment. It can be transported over long distances in the form of aerosols. Air samples are positive for up to two weeks following parturition, and viable organisms are present in the soil for periods of up to 150 days (Marrie, 1990). Research done in the neighbourhood of Helmond (the Netherlands) shows that

persons who live within a radius of 2 kilometre of an infected farm have a thirty times higher risk to become infected compared to people who live outside of this radius. The same study shows that this risk of infection is lower for people living between 2 and 5 kilometres away from an infected farm. The risk of infection for people living further away than 5 kilometres is very low (personal communication by Yvonne van Duynhoven, RIVM).

Diagnosis of Q fever

Diagnosis can be made in two ways: demonstrate antibodies against *C. burnetii* or demonstrate the aetiological agent in tissues, se- and excretions. Antibodies can be demonstrated by a complement fixation test (CFT). In addition, there are several ELISA's available that are usually based on the detection of IgG against a combination of phase I and phase II antigens. Antigens or DNA of the aetiological agent can be detected using biomolecular techniques, like PCR, in situ hybridization, immunohistochemistry or culturing (Muskens et al, 2007).

History of Q fever in humans

History

The first human cases of Q fever were reported in 1933 in abattoir workers in Brisbane, Queensland, Australia. The first attempts to isolate the aetiological agent by inoculating guinea pigs with blood or urine of infected patients were unsuccessful (Derrick, 1937). At about the same time there were also cases reported in America. In 1937 two research teams, one in Brisbane and one in Montana studied the disease and tried to isolate an aetiological agent. They demonstrated that the aetiological agent displayed properties of both viruses and rickettsiae (Burnet and Freeman, 1937; Cox, 1938; Davis and Cox, 1938) In 1938 *Rickettsia diaporica,* the proposed name for the organism (Cox, 1939), was isolated from a cell culture and from incubated eggs. After exchanging information between the two research teams it was concluded in 1939 that *Rickettsia burneti* (Derrick, 1939; Maurin and Raoult, 1999) was the causal agent which was later named *C.burneti* and eventually *C.burnetii*.
After this first documentation of outbreaks in Australia and America, Q fever has been described in many other countries. In 1955 Kaplan and Bertagna working as researchers for the World Health Organisation (WHO) reported that Q fever is present in almost all countries of the world, excluding New Zealand, Poland, Ireland, the Scandinavian countries and the Netherlands (van den Brom and Vellema, 2009).

History in the Netherlands

Between 1954 and 1956 6000 human cases of atypical pneumonia in the Netherlands tested serologically negative for Q fever. The first human cases were seen in the Netherlands in 1956 (Westra et al. 1958). Q fever became a notifiable disease in humans in 1978, resulting in 1 to 32 annual Q fever cases (average 17 cases) in the Netherlands between 1978 and 2006. Between 1994 and 2001 49 people were hospitalised.
In an investigation of Richardus 84 % of 222 large animal veterinarians were seropositive in 1982. In 1983 24% of investigated blood donors were seropositive. (Richardus et al., 1984,). In a sero-epidemiological study performed between 1968 and 1983, occupational groups with a supposedly high risk of infection (veterinarians, taxidermists, residents of dairy farms and female wool spinners) were found to have a significantly higher seropositivity percentage than the control group (Richardus et al., 1987). The conclusion was that Q fever was already endemic for a long time (van den Brom and Vellema, 2009; public statements by P. Vellema, 2009).

Sheep and goat dairy industry in the Netherlands

There have been dairy sheep in the Netherlands for a very long time (Jansen, 1985). They used to be kept in small numbers to supply families or local communities with dairy products. Nowadays the number of dairy sheep per farm differs widely, from less than fifty to almost a thousand.

The dairy goat industry started to increase after the introduction of the milk quota system in the dairy cattle industry in the Netherlands in 1984. Within 25 years the goat population grew from around 3300 goats in 1984 to over 370,000 in 2009. (Table 1) The total milk production grew from almost nothing to over 150,000 tons of milk annually.

	2000	2005	2007	2008	2009
Goats	178571	291891	324014	354878	374184

Table 1: Goat populations in the Netherlands over the years

A large difference between the goat and sheep dairy industry is that goats are usually housed indoors using a deep litter system throughout the year. The deep litter system is an animal housing system, based on the repeated spreading of straw material in indoor booths. An initial layer of litter is spread for the animals to use for bedding material and to defecate in, and as the litter is soiled, new layers of litter are continuously added by the farmer. Another difference is that goat farms are generally larger, up to 5000 animals, than sheep farms.
The sheep and goat industry with around one million breeding ewes and a quarter of a million breeding goats is relatively small compared with other countries (I&R-database 2009). The total number of registered small ruminants farms is a little over 5000, of which 360 are professional dairy goat farms with over 200 adult goats and 40 are professional dairy sheep farms (van den Brom and Vellema 2009).

Q fever prevalence in the Netherlands

Q fever in farm animals in the Netherlands

In 2005 *C. burnetii* was first identified as the cause of abortion on two dairy goat farms in the Netherlands. The diagnosis was confirmed by using immunohistochemistry on sections of placenta (Wouda and Dercksen, 2007; van den Brom and Vellema, 2009). In the subsequent years several abortion outbreaks were demonstrated to be caused by *C. burnetii* (table 2).

	2005	2006	2007	2008	2009	Total
Sheep farms	-	1	-	1	-	2
Goat farms	2	6	7	7	4	26

Table 2: Reported abortion outbreaks in Dutch sheep and goat dairy farms.

The average number of goats per infected farm was 900. On average 20% (10 to 60%) of all goats had aborted. The average number of sheep for the two infected farms was 400 and the abortion rate was 5% (van den Brom and Vellema 2009).

In a recent study, 15772 blood samples of small ruminants which were tested for *Brucella melitensis* were also tested for *C. burnetii* using an ELISA. From those samples, 78% were of ovine and 22% of caprine origin. Based on the research of these blood samples, the seroprevalence in goats is 7,8 % and the seroprevalence in sheep is 2,4 % in the Netherlands (van den Brom and Vellema, 2009; public statements by Vellema, 2009).

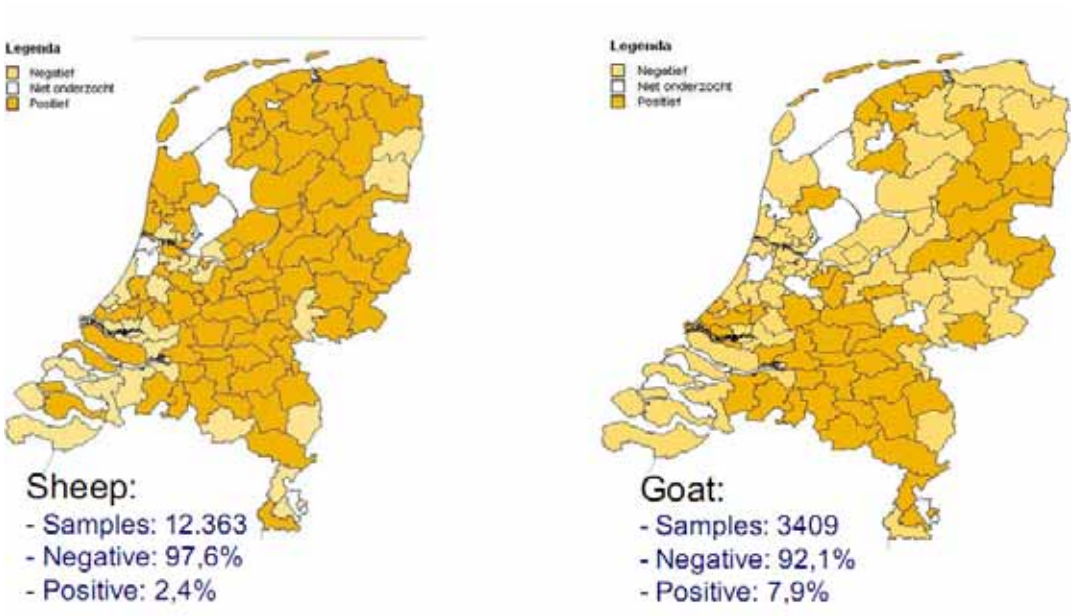


Figure 2: Seroprevalence Q fever 2008

Demonstration of *C. burnetii* using a PCR of tank milk was made mandatory in the Netherlands in October 2009 and showed that 61 farms of the 450 small ruminant dairy farms were infected (Food an Consumer Product Safety Authority,VWA).

During the first Q fever epidemic outbreak in 2007 in Noord-Brabant (the Netherlands) there was a causative connection suspected between the dense population of dairy goats in this area, the high abortion rates and the amount of human Q fever cases. Also the air samples taken in the neighbourhood of infected farms were found to contain bacteria. Experts are now convinced that large dairy goat farms are the main source of the Q fever outbreaks in the Netherlands. Until now eleven different subtypes of the Q fever bacterium are collected, one is found more often on farms with an abortion problem. There are found many similarities between the subtype that is found in human and goats.

Q fever in humans in the Netherlands

Until the end of 2006 there were approximately twenty annual Q fever cases in the Netherlands. Since 2007 there has been a sharp increase of the number of human Q fever cases, with over 2300 confirmed cases of Q fever and six deaths in 2009 (RIVM). These confirmed cases of Q fever resulted in hundreds of clinical presentations of pneumonia, hepatitis, febrile illness and/or hospitalisation.

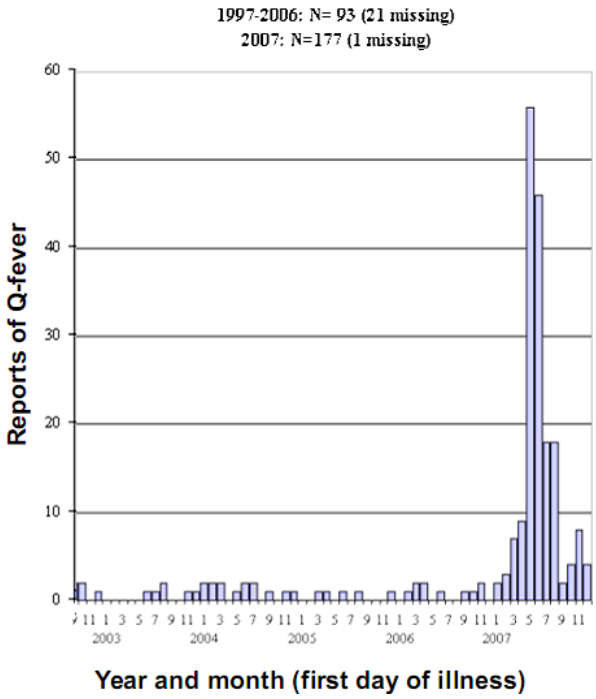


Figure 3: Human reports of Q fever in the Netherlands 2003-2007

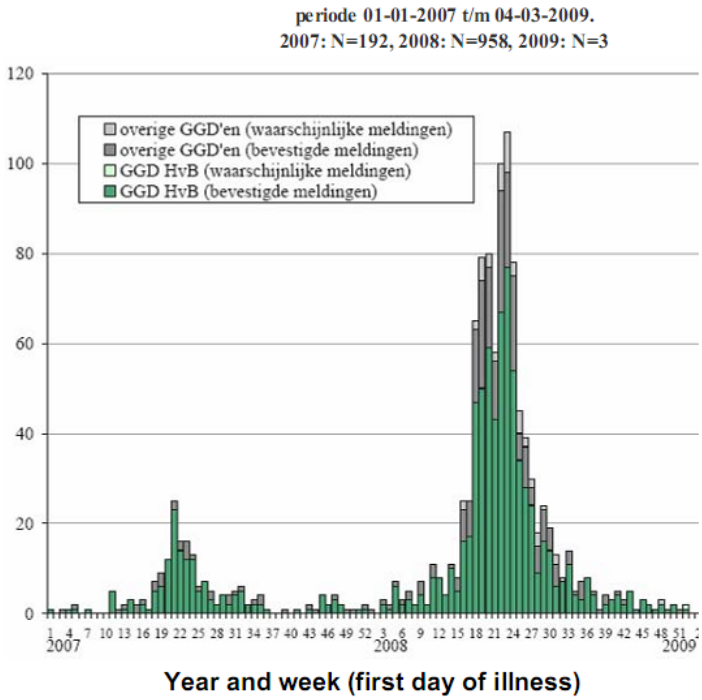


Figure 4 Human reports of Q fever in the Netherlands 2007-2009

Interestingly, in May 2007 a medical microbiologist reported several cases of atypical pneumonia, which were not responding well to antibiotics, to the municipal health service of the province of Noord-Brabant. Four days later a general practitioner in Herpen independently reported an increase in the number of cases of atypical pneumonia in his practice. Two weeks later another general practitioner reported an increase of atypical pneumonia's in his practice in the same region. However, in contrast to the *Mycoplasma pneumonia*, which was first thought to be the source, it was retrospectively shown that *C. burnetii* was the cause of the pneumonia cases (Steenbergen et al., 2007).
At present, human cases of Q fever are reported to the National Institute of Public Health and the Environment (RIVM) if two preconditions are met:

The patient must be diagnosed with one of the following:

- Fever
- Pneumonia
- Hepatitis

Serology of the patient's blood samples must show one of the following: :

- Seroconversion or a fourfold or greater increase in IgG antibodies against *C. burnetii* in a pair of sera (sera taken in the acute phase and recovery phase with an interval of two weeks or more) by indirect immunofluorescence or complement fixation test (CFT)
- Presence of IgM antibodies against phase II *C. burnetii*
- Presence of antibodies against phase I of *C. burnetii* (chronic infection)

Q fever research in the Netherlands.

At this moment, over 30 studies are ongoing in the Netherlands. Different organisations, like the National Institute for Public Health and the Environment (RIVM), the Center for Infectious Disease Control (CIDC), the Animal Health Service (GD Deventer) and the Central Veterinary Institute (CVI) are currently studying various aspects of the disease. Researchers are trying to identify the causal relationship between human cases and infected herds, the different bacterial strains involved, the percentage of herds infected and routes by which they get infected, the environmental resistance of the bacterium, the role of intensive farming methods in the Netherlands, the effects on child birth, the overall sero-prevalence in humans and its course. For more information on Q fever research in the Netherlands,
see: http://www.rivm.nl/cib/themas/Q-koorts/Q-koorts_onderzoek.jsp

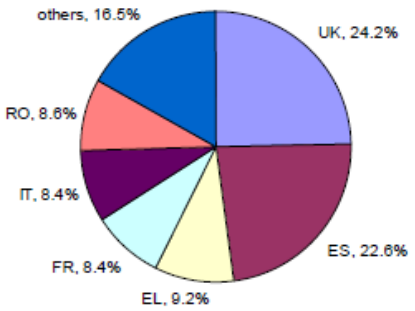
Q fever in Europe

The situation in other European countries

Animals

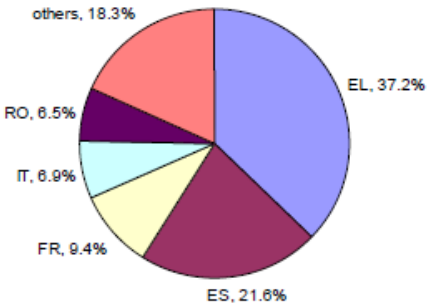
The main EU Member States producing sheep and goats are (Figure 1 and 2): Spain, the United Kingdom, Greece, France, Italy, Romania, Ireland, Bulgaria and Portugal. In a neighbouring country of the Netherlands, Belgium, seven dairy goat farms were officially declared infected (FASFC, Federal Agency for the Safety of the Food Chain).

Figure 1: Distribution of the sheep population in the EU in 2007



Source: Eurostat

Figure 2: Distribution of the goat population in the EU in 2007



Source: Eurostat

Human

EU countries have reported a very small number of human cases of Q fever over the years. Most of these cases were people who had a higher risk because of their profession, such as farmers, veterinarians or people who worked in a slaughterhouse. Incidental local outbreaks around a hundred or less people were reported (Table 2). The situation in several European countries with a recent outbreak or developments will now be described.

Year	Country	Source	Number of patients	Diagnostic Method
2003	Italy	Sheep	133	IF
2002	France	Sheep	88	IF
1999	Israël	Unknown	16	ELISA
1998	Australia	Sheep (abattoir)	33	Serology/PCR
1997	Bosnia	Sheep	26	Serology

Table 2: A few important recent outbreaks of Q fever (Arricau-Bouvery and Rodolakis, 2005)

Earlier literature suggested that the Scandinavian countries were free of Q fever. Recently, there have been publications describing the presence of Q fever in Sweden and Denmark. There have been human cases linked with the sheep industry in Sweden. In Denmark, *C. burnetii* has recently been reported as one of the causes of abortion in sheep. The few annual cases Denmark had, were believed to have a foreign origin. Preliminary reports now describe *C.burnetii* in milk samples of Danish dairy cattle. Serum samples of al large cohort of farmers, veterinarians, inseminators and hoof trimmers, all having occupational contact with dairy cattle, were tested for the presence of immunoglobulin G to phase I and phase II antigens of *C.burnetii.* In 39 of 329 study persons (11%) the presence of antibodies to *C.burnetii* was found. Veterinarians had the highest seropositivity rate (36%). This survey suggests that *C.burnetii* is a recently acknowledged domestic infection of Denmark and that the risk of infection is associated with occupation (Bosnjak et al., 2009).

In Germany, especially in Baden-Württemberg, Bavaria and Hesse, the number of human Q fever cases more than doubled compared with the last 5 years. This increase is not only seen

in human cases but also in sheep and goats. In 2007 and 2008 respectively there were 83 and 370 human notifications (Jahresstatistik, 2008; 30)

In 2008 a seroprevalence study done in three provinces in Turkey showed a overall 20% seroprevalence in the 42 flocks tested (n=151). A total of 34 flocks (81%) revealed at least one seropositive animal (Kenneman et al, 2008).

In the Basque Country (North Spain) a study was carried out combining bulk tank milk PCR and antibody level determination to estimate the prevalence of *C. burnetii* in the dairy sheep population in 2008. Of the analyzed flocks 22% were PCR positive and of the individually testes ewes 8,9% of the animals showed serologically positive. At least one seropositive ewe was found in 67,6% of the flocks (Garcia-Perez et al., 2008).

In 2007 a screening program for the presence of *C. burnetii* in bulk milk samples from cows, goats and sheep and shell eggs produced in and imported into Switzerland was conducted. In total 17 of 359 (4,7%) of analysed bovine milk samples from two randomly selected cheese dairies were tested positive for *C. burnetii* with PCR. 81 ovine and 39 caprine bulk milk samples were all tested negative for *C. burnetii.* The 504 shell eggs tested were also found to be negative for *C. burnetii* (Fretz et al, 2007).

In 2004 there was a Q fever outbreak in a homeless shelter in Marseille reported, the main factor was probably an abandoned slaughterhouse (Brouqui et al., 2004).

In the context of their work on gathering and sharing information on zoonoses in different EU Member States, EFSA and ECDC collected data on occurrence of Q fever in animals and humans. The information is published in the Annual Community Summary Report on Zoonoses and Food-borne outbreaks for 2008.

Q fever cases in humans were analysed for the first time at European Union level in 2008 and a total of 585 confirmed cases were reported in 2007 with the number of cases increasing to 1,594 in 2008. Q fever was also recorded in cattle, goats and sheep. The highest infection rates were reported in goats, increasing from 9,7% in 2007 to 15,7% in 2008. (EFSA)

Q fever management

The Netherlands

Measures taken by the Dutch government and other stakeholders

Government measures are aimed at the dairy goat and sheep industry. Because meat-producing sheep are kept in less dense populations, they are considered not to be associated with public health risks. The same applies for animal farms for children and small farms (less than 50 animals).

Measures before 2008:

Abortion outbreaks were reported on a voluntary basis to the Animal Health Service (GD Deventer) and confirmed by immunohistochemistry before June 2008, after which additional measures were taken (Wouda and Dercksen, 1997; Van den Brom and Vellema, 2009).

Measures taken in 2008:

- Notification obligation for goat farms and sheep farms in case of high abortion rates:
    - Farms with less than 100 animals, 3 abortions within 3 days.
    - Larger farms, more than 5% abortion of pregnant animals within 30 days.

- When a farm was found to be infected, no visitors were allowed in the fold for three months and no manure was to be removed from the fold for three months.
- Vaccination was voluntarily in 2008.

Autumn 2008, approximately 35.000 goats were vaccinated with Coxevac (Ceva Sante Animale) a Phase I vaccine containing inactivated *C. burnetii* (Van den Brom and Vellema, 2009).

Measures taken early 2009:

Notification obligation for goat farms and sheep farms in case of high abortion rates (same as in 2008)

- Compulsory vaccination of 'high risk goat farms and sheep farms' of the Netherlands
- Voluntary vaccination in the rest of the Netherlands
- Hygiene protocol, which is in part mandatory
- Further research

Explanation:
Vaccination against Q fever is mandatory for dairy goat farms and dairy sheep farms with more than fifty animals in a large part of the South of the Netherlands. This part of the Netherlands is considered a risk area because of the many large dairy goat farms in densely populated areas. For farms with a public function or farms with a Q fever outbreak reported by the Food and Consumer Product Safety Authority (VWA) vaccination is mandatory. For farms outside this area or with less than fifty animals vaccination is still voluntary.

In the summer of 2009 it was dicovered that PCR on bulkmilk gave a good indication of infection on farms. On 1 October 2009 bulk tank milk research started. Every farm with more than 50 dairy goats and dairy sheep is required to take a bulk milk sample to investigate for the presence of *Coxiella burnetii.* The research is conducted by the Animal Health Service (GD Deventer). A positive outcome is reported to the Food and Consumer Product Safety Authority (VWA). The Food and Consumer Product Safety Authority (VWA) then visits the farm and takes a sample of bulk milk and vaginal swabs from a number of animals. These are sent to the Central Veterinary Institute (CVI Lelystad) for confirmation. When the presence of the bacterium *Coxiella burnetii* is confirmed by the CVI a farm is considered to be contaminated. The bulk research method replaces the so-called "5% criterion".

Additional measures for infected farms:

- No manure may be removed from the stable between the start of the lambing period and thirty days after the end of the lambing period.
- Removed manure is stored and covered for ninety days at the site where the manure is produced. Records are kept of the date of the removal of the manure from the stable, the beginning and the end date of the composting period on the location and the date of spreading the manure on the farm.
- There is a requirement for infected farms to adequately control vermin. Also there needs to be sufficient bins available in the stable to put in placentas and abortion material.
- It isn't allowed to move animals to other milk producing farms.
- Infected farms may only buy animals from farms which are not contaminated and the animals must be vaccinated.
- No visitors are allowed.

Measures 2010

- Mandatory vaccination for all dairy goat and sheep farms with more than fifty animals and farms with a public function. Wanneer is dit besloten?
- Culling

Explanation:
In October 2009 the Ministry of Agriculture instructed a group of researchers led by Mr. Coutinho of the National Institute for Public Health and the Environment (RIVM) to devise and compare additional measures. It is their task to evaluate how effective these potential control measures should be. Possible measures comprise:

a) To remove dairy goat farms and dairy sheep farms from residential places
b) To cull all dairy goats and dairy sheep and to desinfect infected dairy goat farms and dairy sheep farms
c) To cull only the infected animals on infected dairy goat farms and dairy sheep farms
d) To remove all dairy goats and dairy sheep on farms within a 5 kilometre radius of a residential or recreational area
e) To impose a breeding ban on infected farms, and whether or not to prohibit milking in the meantime
f) To reduce drift of bacteria: closing the infected farm with wind stopper
g) To prevent drift of bacteria: completely windproof infected farms

On 16 December 2009 Agriculture minister Gerda Verburg and health minister Ab Klink of the Netherlands decided to cull all pregnant goats on infected farms, vaccinated farms and non-vaccinated farms. Originally it was planned to make a distinction between infected and non-infected animals and between vaccinated and non-vaccinated farms while culling pregnant animals on infected farms.
But according to experts it is not possible to make an absolute distinction between infected animals and non-infected animals on these farms. The risk of obtaining false-negative results by testing one sample at one moment before an abortion or normal delivery is considered to be too great. All male goats on infected farms are also culled because of the risk Q fever transmitted through infected semen.
Experts have advised that the movement of pregnant animals to a slaughterhouse is undesirable both for animal welfare and public health reasons. The risk of abortion while in transit is unacceptable. This would also form an unnecessary health risk for transporters, slaughterhouse personnel and people living in the neighborhood. Therefore, the animals are euthanised by lethal injection on the farm and then go for destruction.

The culling campaign started on Monday, December 21 2009, and will cover 34.500 pregnant animals and over 1200 male goats on 55 infected farms. The non-pregnant female animals will be kept alive, but cannot be used for breeding purposes anymore during their lifetime. On 17 December it was announced that another 5 farms were infected. Authorities plan to cull an extra 5000 goats on top of the 35 000 earlier announced.

On 23 December it was announced that at that moment a total of 61 farms were infected. It is expected however that more farms are infected, as goats excrete the bacterium intermittently.

Farmers are financially compensated for their culled animals.

At the same time, the Dutch Farmer's Association (LTO) presented an action plan in November 2009 supported by many dairy goat and dairy sheep farmers. This action plan contained scientifically proved measures to reduce the zoonotic spread in the area of farms that were considered to be infected. Part of these measure were for example milking for 2-4 years without lambing in the meantime, individual testing of animals, screening of positive animals and a voluntary arrest of farm growth for at least one year in areas with a high rate of human infections.

Additional Measures 2010:

Bulk milk research

A higher frequency of mandatory tank milk testing for the presence of *Coxiella burnetii* (once every two weeks) for all holdings with 50 dairy goats or dairy sheep and more has been established.The holding is to be regarded as suspect after one positive sample. After a positive result in confirmation testing by the CVI, the holding is declared infected.
The Animal Health Service (GD, Deventer) examines bulk tank milk samples for the presence of Coxiella burnetii. In most sheep and goat farms, these samples are collected by the Animal Health Service (GD). Some farmers, however, send their samples to the Animal Health Service (GD) independently. Following the modification in the regulations, the Animal Health Service (GD) will collect samples from these farms directly, similarly to all other farms. By this arrangement, the quality of the samples and the reliability of the research results will improve. This regulation addresses about 50 out of the 411 sheep and goat farms. The changes took effect on 30 Dec 2009, at 4.00 pm.

Notification

Based on national legislation all farmers, veterinarians and other persons involved have to notify symptoms of a contagious animal disease to the competent authority. After notification of a suspicion based on abnormal abortion numbers, the competent authority will visit the farm and take a sample of the tank milk. If the milk tests positive for the Q fever bacteria, the farm is declared infected.

Suspension of expansion

All farms with more than 50 dairy sheep and dairy goats will not be allowed to expand beyond the reference number of the November 2009 census and can only bring in vaccinated animals. The reason for this measure is that animals do not continuously secrete the Q fever bacteria, which makes it impossible to recognize all infected farms in time. It is expected to find more infected farms in the coming months until the end of the lambing period.

Ban of breeding

Although most animals have been mated already, a general ban on breeding for all farms with 50 or more dairy goats or dairy sheep has been established until July 1 2010. This again has to do with the fact that the bacteria are secreted intermittently, which means that some of the farms which are currently not infected may become infected later on. On such farms, pregnant animals will have to be culled and the aim is to minimize that number.

Manure- and hygienic measures.

On infected farms it was already prohibited to remove the manure during the lambing period until 30 days after the end of the lambing period. After 90 days of covered storage, the

manure was allowed to be spread on the land. For infected farms there will now also be a ban on manure removal from the moment of culling the animals until 30 days after. The other measures will remain in place. Because farms, which are currently not infected, could become infected in the next couple of months, the manure and hygiene measures will now be in effect for all other dairy goat farms and dairy sheep farms. All farms will have to store the manure under cover on the farm before moving it away from the farm.

Visitors

As of June 2008 infected farms are not allowed to receive visitors. People visiting the farm stables in a professional capacity are exempted.

Transport restrictions

As on 1 October 2009 infected farms cannot move animals to other farms, which supply milk. Animals were allowed to be moved to a slaughterhouse, while young animals could be moved to a fattening farm. In addition to these measures for infected, we now also prohibit the movement of young animals to breeding farms.
Infected farms can only bring in vaccinated animals from non-infected farms. We have now expanded this measure to all non-infected farms i.e. all farms can only bring in vaccinated animals.
On Friday 18 December 2009 the Minister of Agriculture announced that all transport of dairy sheep or dairy goats to farms, which supply milk, is prohibited until 1 July 2010. Only transport to fattening farms or directly to slaughterhouses is still allowed.

Other farms with sheep and goats

The measures on commercial dairy goat and dairy sheep farms are far reaching in order to prevent the secretion of too many bacteria. Q fever may also occur in other sheep and goats, such as on animal farms for children, and in other species of animals, such as cats, bovines and horses.
Experts have told that the cause of the outbreak can be found in the commercial dairy goat and dairy sheep sector. Therefore, all measures taken are aimed at this category. The government, however, closely monitor the situation in other establishments and other types of animals. They will also seek further scientific advice about the possible risk associated with animal farms for children and other types of public facilities with susceptible animals present.

Reactions by stakeholders

The Dutch Farmers Association LTO has said it rejects the killing of healthy goats to fight the spread of Q fever.
It is not clear whether LTO will take action against the government decision.

The Royal Dutch Veterinarian Association (KNMvD) is very disappointed about the decision to cull all the goats on ethical grounds, but does understand it at the base what is known by now. They will however make sure that the culling process will be carried out very carefully.

How Europe responded to the Dutch situation

For the prevention and control of Q fever there is no legal basis to start with, the only thing that can be done now is notification if there is an outbreak somewhere, but this is on voluntary basis. The Netherlands reported two times officially to DG SANCO during the Standing Committee on the Food Chain and Animal Health (SCoFCAH) meeting on 6 May and 3 November.

The EU commission carefully follows the news of the Netherlands ("Passive surveillance"). A request has been prepared for the European Food Safety Authority (EFSA) to make a risk assessment. EFSA's Panel on Animal Health and Welfare (AHAW) will lead the work with the support of the Panel on Biological Hazard Panel (BIOHAZ) and in close collaboration with the European Centre for Disease Prevention and Control (ECDC). A scientific opinion is expected by the end of April 2010. The Panel will look at the occurrence and spread of Q-fever in farm animals and humans across the EU, assess the risks factors related to the disease, as well as evaluate the effectiveness and efficiency of disease control options. These may include vaccination, animal movement and biosecurity restrictions and pharmaceutical treatments. (EFSA)

Coxiella burnetii is a bacterium endemic in the environment of whole Europe. It is thought that Q fever is a national problem in the Netherlands, because of the kind of animal housing systems they have for goats, deep litters.

Another reason why it is thougt that this problem is seen in the Netherlands, is the fact that many people live in the close neighbourhood of large farms. A situation not much seen in other countries.

Discussion

The outbreak in the Netherlands is by far the largest community outbreak of Q fever ever reported in the literature. Until 2007 only fifteen to twenty annual cases of Q fever in humans were reported in the Netherlands. In 2007, 2008 and 2009 respectively there were 168, 1000 and over 2300 reported human cases in the Netherlands.

It has been suggested however that the amount and severity of cases was significantly under-reported before 2007. It has been argued that the alarmed status of the Dutch health service since 2007 and the subsequent increase in the number of blood tests carried out was responsible for the increase in the number of Q fever cases. Under-reporting of Q fever in the Netherlands has already been suggested in 2003 using the sero-epidemiological study of Richardus et al. published in 1987 (Van Gageldonk-Lafeber et al., 2003). However, the same organisation, the National Institute for Public Health and the Environment (RIVM), now states that under-reporting couldn't have been the cause for the sudden increase in Q fever cases. In a more recent study they showed that only 2% of the Dutch population was sero-positive for Q fever using blood samples from 2006 and the beginning of 2007. This suggests a low incidence of the disease before 2007.

Because of the high numbers of *C.burnetii* bacteria shed after an abortion, the high abortion rates and the fact abortion waves and human cases were found in the same area, dairy goat farms are believed to be the main source of the Q fever outbreaks in the Netherlands. (van den Brom and Vellema, 2009) The connection is still indirect and based on epidemiological research of data from Herpen, Helmond and in Limburg (the Netherlands). Until now eleven different subtypes of the Q fever bacterium are collected. One of the subtypes is found more frequently in infected goat farms in the Netherlands. There are found many similarities between the subtype that is found in human and goats. This suggests that dairy goats are the main source of human Q fever outbreaks in the Netherlands.
Interestingly, meat-producing sheep aren't considered to be a great risk for public health. They are kept extensively, in less dense stocks. Furthermore, small stocks (less than 50 animals), such as those found on animal farms for children or small farms are not seen as a great risk for public health. Remarkable is however that two human Q fever cases could presumably be traced back to an animal farm for children, as thirteen of the nineteen goats were found to be positive for *C.burnetii*. However, the combination of the ubiquitous presence and the high sensitivity of the test used to test these animals makes it impossible to conclude whether there is a true public health risk.

It is difficult to assess to what extent the present Q fever outbreak is typical for the Dutch situation and what the risks for other European countries are. In other European countries, like Denmark and Germany there has also been an increase seen in human cases of Q fever, but not to the same extent as in the Netherlands. An expert of the Animal Health Centre (GD Deventer) is of the opinion that this is caused by less accurate observations by the surrounding countries themselves. According to the expert, it's quite remarkable that the problem "stops" exactly at the border.

In Bulgaria, because of big political and economic changes in the beginning of the 1990's, the number of goats almost tripled, the contact between goat owners and goats increased, the contact between other animals and goats increased and the consumption of raw goat products increased. As a consequence, goats, instead of cattle and sheep, became the main main source of human Q fever infections. The developments in Bulgaria led to an increase in the number of confirmed human cases. (Serbezov et al., 1999).In this same article is concluded that goats may pose a threat to human health as a source of *C.burnetii* infection in every country in which they are raised extensively and are in close contact with humans,

It is hypothesized that the outbreak in the South of the Netherlands is typical for the Dutch farming situation. Despite the relatively small goat population in the Netherlands, there has been a sharp increase in the number of goats after the introduction of the milk quota system in the dairy cattle industry in 1984. It has been argued that the presence of large dairy goat farms in the middle of a highly populated area is typical for the Dutch situation and a cause for the outbreak.

In addition, most goats are kept in deep litter systems in the Netherlands. Experts think that this system provides a good basis for the spread of *Coxiella*. One theory is that infected material like placenta's dry in the deep litter, eventually forming aerosols and infecting inhabitants in the surrounding area. In one example, there have been no reported human Q fever cases in the surroundings of a *C. Burnetii*-positive dairy goat farm. It is remarkable that this farm is using slatted floors instead of the deep litter system (Personal communication, J.van Steenbergen). Although this example doesn't provide us any statistical evidence, it forms another indication that the deep litter system is a cause for the Dutch problem.

As the dairy goat and sheep industries were considered the main source for the human Q fever outbreak in the Netherlands, the Dutch government has taken many measures aimed at these sectors since 2008. Most drastic actions were taken at the end of 2009, with the decision to cull all pregnant and male animals on infected farms.
Despite the finding that dairy goat farms don't form the only source for Q fever in the Netherlands, the ministry of Agriculture decided not to take any measures against for example the infected animal farm for children. It was even allowed to breed with the existing animals present on the farm. This uncomprehended government decision caused the mayor together with the municipal health service to decide to close the animal farm for the public.

The question arises whether the surveillance systems are adequate. The National Institute for Public Health and the Environment (RIVM) says that there has to be a better surveillance system, as signals are coming through too late. The Ministry of agriculture on the other hand says that the surveillance systems on paper are better than in many other countries, but that they're not used properly.
Moreover, there are conflicts of interests as all players in the game to prevent Q fever have a different starting point. For example, animal farmers often don't benefit from reporting animal diseases. They don't see the necessity to report or there is a threshold to overcome. Veterinarians have a relationship of trust with animal farmers, but also have to keep an eye on zoonotic diseases. As a result, disease notification is done either too rarely or too late.
It is needed to recognize these and more conflicts of interests and to work with them.

The Netherlands is a very densely populated area and there have been many large animal disease outbreaks in the last couple of years. In 1997 there were classical swine fever and BSE, in 2001 Foot and Mouth Disease and in 2003 Avian Influenza. It has been suggested that Dutch animal farming, a very intensive method, is inextricably bound up with animal disease outbreaks. Other opinions are that there is no immediate need to discuss the intensive farming method. The hype-driven, emotional discussions don't form a proper base to evaluate the built-in disadvantages of intensive farming.
Anyhow, the Dutch Ministry of Agriculture states that the Q fever outbreak isn't a reason to start a debate on the justification of intensive farming method in the Netherlands. At the moment research is ongoing by the Institute for Risk Assessment Sciences (IRAS, Utrecht University), the Netherland's Institute for Health Services Research (Nivel), and the Centre for Infectious Disease Control (CIDC) to assess whether intensive farming plays a part in the problems with Q fever.

Conclusion and recommendations

The recent Q fever outbreak in the Netherlands has never been seen before and instigated a large multidisciplinary research portfolio as many questions are still unaswered.

It is now thought that the Dutch situation provides the right conditions for an outbreak: large dairy goat farms using the deep litter system situated in areas with a high population density. Interestingly, no human Q fever cases were found in the surrounding of the only dairy goat farm in the Netherlands using slatted floors instead of the deep litter system. As deep litters are considered to be at the root of the current problems, it would be interesting to study the consequences of using this system compared to the system using slatted floors.

Since large dairy goat (and sheep) farms are considered to be the main source of the Q fever oubreaks in the Netherlands, goverment measures were and are aimed at these sector(s). Measures that were taken are for example: notification obligation for high abortion rates, vaccination, hygienic measures and a breeding ban. The most drastic action was taken at the end of 2009, with the decision to cull all pregnant and male animals on infected farms.

Although experts agree with the current measures of the Dutch government, it is confusing for both local authorities and the public that infected animal farms for children are left undisturbed. Two human cases could be traced back to an animal farm for children and it's therefore the public opinion that these sources should be included in the government policy plan.
Unfortunately, the Netherlands have a rich history of animal disease outbreaks in recent years. It has been argued that there is a need to evaluate the intensive methods of farming used in the Netherlands in general and especially in densely populated areas, as it has been suggested that these methods are inextricably bound up with risks (research ongoing, results expected in 2011).

It's difficult to assess what the public health risks are for Europe and what systems are needed to minimize these risks. At this moment Q fever doesn't form a big problem in other European countries to the same extent as in the Netherlands. Although it would be a wise thing to monitor the situation closely.

It seems both useful and important to properly study the situation in the Netherlands. The data can subsequently be used to prevent spread in Europe and other countries can use it as a guideline to develop prevention and control measures. There are several regions in Europe were there is a similar situation as in the Netherlands: large dairy goat farms in the neighbourhood of a densely populated area (Personal communication, Yvonne van Duynhoven, RIVM). Bavaria in Germany for example, has regions comparable to the Dutch Q fever regions. There has already been a twofold increase in the number of human Q fever cases in Bavaria in the past 5 years.

For a surveillance system to be effective it is important that key players collaborate openly with each other. Although the involved players have conflicting interests it is essential that veterinarians, doctors, farmers, researchers and veterinary and public health institutes share information. Optimizing animal health and minimizing public health risks can only be assured by working together.

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Interview with experts

1) Sanna Mesman - European Commission
2) Carian Posthumus Meijes - Ministry of agriculture
3) Yvonne van Duynhoven - National Institute for Public Health and the Environment (RIVM)
4) Piet Vellema - Animal Health center (GD Deventer)