

PATHOGENIC STRAIN OF BACTERIUM UNIQUE TO THE NETHERLANDS

Q fever raises many questions

The outbreak of Q fever in the Netherlands may stem from a strain of bacteria that is unique to the country, according to a research by the Central Veterinary Institute (CVI), part of Wageningen UR. The CVI is avidly looking for answers to the many questions surrounding Q fever.

TEXT BROER SCHOLTENS ILLUSTRATIONS SEBASTIAAN DONDERS

The Q fever bacterium *Coxiella burnetii* has been around for years in the sheep and goat sector without affecting humans much. That has changed: this animal disease is now causing big problems. The Central Veterinary Institute (CVI), part of Wageningen UR, has significantly expanded its basic research on Q fever in the past year, in response to the explosive nature of the disease outbreak. This explosion seems to be affecting the Netherlands alone – nowhere else, not even Australia, the ultimate sheep and goat country. To explain this, new research points to a unique and virulent bacterial strain that is only circulating in the Dutch goat sector. But how did this strain get here? The outbreak is also being put down to the massive rise in the number of goats

in the Netherlands in the past 25 years. Research into the origins and distribution of the disease is in full swing, and should provide answers about the best strategy for halting the disease and preventing further infections. Will vaccinating all goats, for example, spare human beings from infection?

FROM GOAT TO HUMAN

Veterinarian Fred van Zijderveld is head of the bacteriology department at the CVI in Lelystad. Besides Q fever, he is interested in rare diseases such as ‘mad cow disease’ and scrapie, a disease which affects the central nervous system in sheep. Van Zijderveld is a busy man. And he is on duty, so his mobile phone rings quite frequently. ‘Fine, send in the samples, we will have a look at them’,

he tells a caller. ‘That was the zoo’, he then explains.

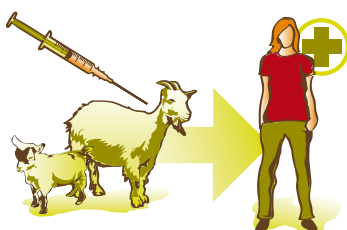
The origin of this infectious disease has long been a mystery, which is why it is called ‘Query fever’. It is now clear that humans catch the disease from dairy goats and sheep. The Q fever bacterium is seldom transferred from person to person; it mainly affects people who come into contact with infected animals, or who live near goat farms. Eighty percent of vets and livestock holders and their families have been infected by the bacterium; this can be seen from antibodies in their blood. ‘They have been sick without having any symptoms; most of them did not notice that they were infected’, says Van Zijderveld. The same research, conducted two years ago by the CVI and the National Institute for Public Health and the Environment (RIVM), >



What is the best strategy for controlling the disease and preventing infection?



Will vaccinating all goats protect people from infection?



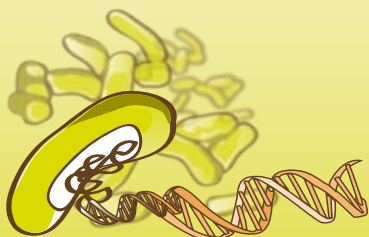
Does it help to vaccinate people?



What is the genetic make-up of the Q fever bacterium?



What information can it provide on the spread and virulence of the disease, the infection process and building up immunity?



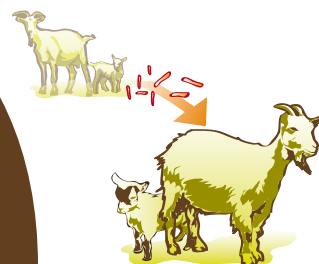
Q fever



How does the infection spread among goats?



How is immunity built up?



What causes the high abortion rate among infected goats?



Infected cattle and pigs have very few symptoms. Why is that?



Q fever is only spreading rapidly among goats in the Netherlands. How come?

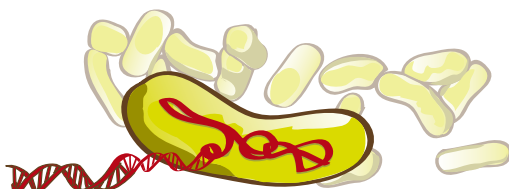


Is it partly to do with the massive increase in the numbers of goats in the Netherlands?





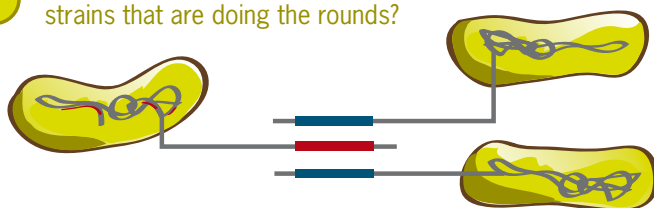
The outbreak of Q fever in the Netherlands may be due to a unique bacterial strain that only occurs on Dutch goat farms.



How did the strain get here?



How does this strain differ from the other strains that are doing the rounds?



SHOULD PEOPLE BE VACCINATED?

To halt the spread of Q fever, all sheep and goats are being vaccinated and culls are being carried out on dairy sheep farms. The Health Council is researching the usefulness of human vaccination. There is only one human vaccine, which was developed from an Australian bacterial strain and only registered on the Australian market. This vaccine protects 83 to 100 percent of those given it for at

least five years. The Health Council is examining whether high risk groups such as heart patients should be vaccinated. The problem is that very little is known about the possible side-effects of vaccines for these high-risk groups. In Australia it is mainly young, healthy people who are vaccinated. Extensive human vaccination does not seem a viable option at present, due to possible side-effects – some of them serious.

showed that 30 percent of veterinary science students have at some point been in contact with the bacterium. The more often you walk around goat farms, the bigger your chance of infection, concludes Van Zijderveld.

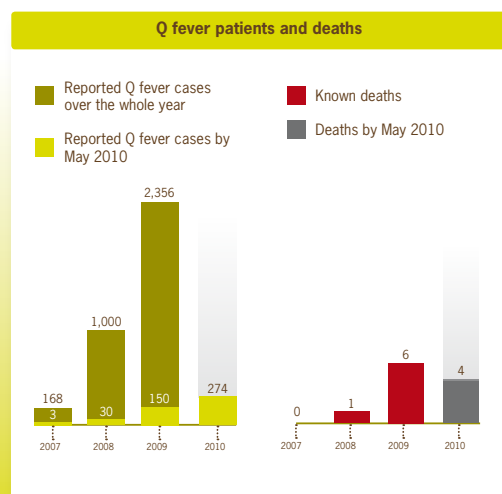
CONDENSED LAYER OF MANURE

Many experts think that the rapid rise in the number of Q fever patients in the Netherlands can be traced to its intensive livestock farming practices, with large numbers of animals per square metre. In 1984 there were 3,300 dairy goats in the Netherlands, most of them on small farms. By 2008 there were 355,000 dairy goats on 400 farms, according to CBS statistics. Most of these farms are in North Brabant between Den Bosch and Eindhoven; the second biggest goat-farming region in the Netherlands is Gelderland.

The most common goat breed is the white Saanen goat, the best dairy goat in the world, with a milk production of over 1,000 litres per year. The animals are kept in deep litter stalls, considered in the goat sector to be relatively animal-friendly. Goat farmers do not use the sorts of animal-unfriendly metal grid flooring common in pig and cow sheds. A deep litter stall is a bit like a swimming pool filled up with straw and goat manure. The animals, on average one goat per ten square metres, walk around and excrete the whole day on straw that is added to daily. At lambing time, they also leave behind amniotic fluid, placentas and aborted fetuses. The doors of a deep litter stall are left open for ventilation so that wet straw dries fast. Once or twice a year, when the condensed layer of manure reaches the top of the stall - by which time it is often 60 to 80 centimetres deep - it is shovelled out. Until recently, it was then spread over the land as fertilizer. Once on the fields, the manure dries out even more, and the bacteria, baked onto clods of manure and soil, are blown with the wind. They can spread over great distances, sometimes up to several kilometres

Farms affected by Q fever

- Farms declared infected in 2009
- Farms declared infected in 2010
- Farms declared free of Q fever in 2010



Sources: OSIRIS/RIVM • CBS • Food & Consumer product Safety Authority

from a goat barn. People living in the immediate vicinity of such barns therefore regularly breathe in Q fever germs which can make them ill.

GERMS TRAVEL

Most cases of Q fever occur in central Brabant, where the most goat farms are located. 'Our guess is therefore that in the Netherlands, Q fever is spread by the wind carrying manure and dust', says Van Zijderveld. 'There is a broad consensus on this.' In wet areas with lush vegetation, the germs will not travel as far as in dry areas with sparse vegetation, such as arable fields. This is probably because vegetation retains dust and germs better. Fewer people will therefore be infected in wetter areas, according to recent calculations by researchers at the RIVM and FutureWater, a Wageningen-based advisory bureau. FutureWater, set up

'If we vaccinate over the next three years, dairy goats will no longer pose a risk to public health'

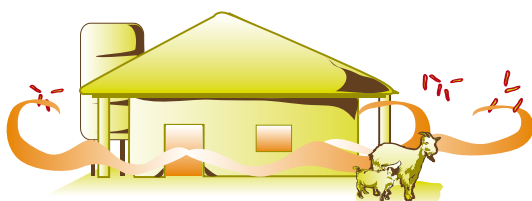
by researchers at Wageningen University, has also found correlations between the number of Q fever patients and the number of spontaneous abortions in goat barns in the neighbourhood.

The reason for this is that the most bacteria get into the manure in the stalls during lambing season, and from there into the air. Spontaneous abortions, which are common in goat barns, are the biggest source of bacteria: when a dairy goat miscarries, billions of bacteria are released into the straw. Even during a normal birth, many bacteria end up

in the deep litter stalls – several million, according to research.

Moreover, it is precisely the *Coxiella burnetii* bacterium that causes spontaneous abortions among dairy goats. Since the Q fever bacterium began to spread faster, the number of such abortions has risen: a vicious circle. There are now barns in which 30 to 60 percent of the infected, pregnant dairy goats miscarry. Van Zijderveld: 'Cattle that are infected with the Q fever bacterium also have the occasional spontaneous abortion, but far fewer than the dairy goats.' ➤

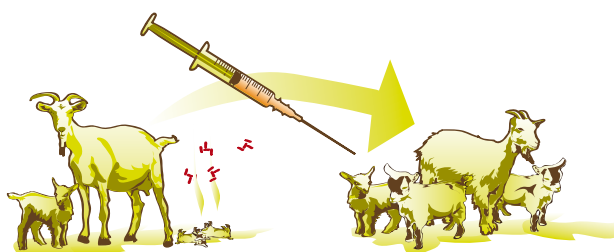
- i** Most bacterial germs get into the manure during the lambing season, and spread into the air from there.



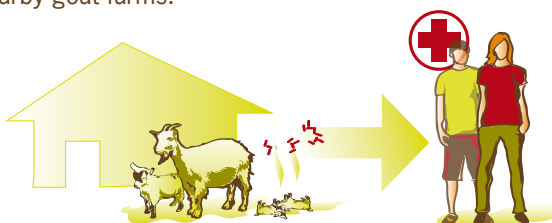
- i** Goats get infected through nose and lungs.



- i** Vaccinating goats cuts the number of abortions almost to zero.



- i** A link has been found between the number of Q fever patients and the number of abortions on nearby goat farms.



The Q fever bacterium is in circulation in the pig sector too, but without many symptoms. The theory goes that these are other, less virulent strains which do not affect the animal so badly.

STORING MANURE AND VACCINATING

Measures currently being taken against the Q fever explosion are primarily intended to reduce the production and airborne distribution of pathogens. For the first time this year, for instance, all sheep and goats are being vaccinated. There were vaccination campaigns during the past two years too, but they often did too little too late. Recent research has shown that vaccination reduces the number of abortions almost to zero. Van Zijdeveld: 'If we vaccinate for the next three years, there will no longer be any dairy goats in the population that pose a major risk to public health.'

Hygiene measures are being introduced to reduce the airborne spreading of dust from manure. For example, a rule that requires manure to be composted for three months before being spread on the fields. During composting, the temperature of the manure rises above 70°C, killing off the bacteria. Research is ongoing to determine exactly how fast the temperature rises in a dung heap, and where in the heap it rises. A further measure being taken is to cull the herds at infected dairy goat farms until June this year, in order to prevent germs from spreading in the short term. With all these measures, the expectation is that the Q fever outbreak will die down. 'There are no other short-term measures', says Van Zijdeveld.

A REMARKABLE FINDING

In the long term we shall have to rely on knowledge generated by new basic research that has been set in motion over recent months, says Van Zijdeveld. For instance, researchers are studying in the laboratory how the infection process works in goats, from contamination to the subsequent building up of immunity. Research is also being done

into the genetic make up of the Q fever bacterium. Several specimens from infected humans and animals have already been analysed genetically, and the initial results are very informative. Fifteen different strains of the Q fever bacterium have been found in the Netherlands to date. Thirteen of these occur in goat barns. But genetic research has now revealed that one type is dominant and, what is more, this type is found hardly anywhere else in the world. 'A remarkable finding, which must mean something', says Van Zijdeveld. 'This might explain the remarkable explosion of Q fever in the Netherlands, and its pathogenic potential among humans.'

The same genetic analysis has been made on blood samples from dairy goats after a spontaneous abortion. In 238 of the 251 samples analysed, the same bacterium type was found: a type that was not found in cattle or sheep, and which does not occur in other countries.

GOATS ARE LIKE TOP ATHLETES

The bacterial strain circulating among Dutch dairy goats seems to be different from those affecting other animals. 'We are trying to find out whether the Q fever bacterium has changed over the years, and whether any change has anything to do with intensive livestock farming. These goats are like top athletes. They have been bred for higher milk production, and this subjects them to a lot of stress and brings them close to their physiological limits', says Van Zijdeveld. 'It could be that this genetic change in the bacterium is responsible for the rising number of abortions among dairy goats in the Netherlands. It is a change that could also have influenced the virulent nature of the disease, and its capacity to make people ill.' The CBI now has eight recent bacterial samples from people, goats and sheep at its disposal. More samples will be added over the coming months, including some from other animal species. The plan is to map the whole genome of all these various Q fever bacteria, and then use bioinformatics tech-

niques to look for genetic differences that could explain the differences in virulence, for example.

BUILDING UP IMMUNITY

The CBI is also conducting tests to identify the infection route. These have included tests over the past few months to find out by which route dairy goats become infected. Twelve dairy goats have been brought into contact with the dominant type by various routes: via the mouth, the nose and the lungs, and by injecting bacteria into the skin. 'Results from this research suggest that inhalation through the nose and lungs is the most likely infection route', says Van Zijdeveld.

'Taking this as our starting point, we are going to scale up the testing this year to include dozens of goats. We shall look again at the infection route via nose and lungs, so as to verify our hypothesis. We shall also look at how the body responds to infection, in order to find out how a goat gradually builds up immunity to the Q fever bacterium. The CBI is also researching how vaccines protect against abortions. 'This sort of information makes it possible to put better measures in place for preventing infections among goats', says Van Zijdeveld. ■



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deputy director of the
Central Veterinary Institute,
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Lelystad.

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EPIDEMIC PROPORTIONS

The outbreak of Q fever has reached epidemic proportions in the Netherlands. Until 2007, GPs were reporting an average of 20 cases per year to the regional health services (GGDs). In 2009, 2,365 cases were registered. In the first months of this year, this rise seems to have continued, albeit on a more limited scale. Up until mid April, there were 243 reports of Q fever. Over half of these patients contracted the disease this year; the others contracted it last year. The figures are distorted, thinks the RIVM (National Institute of Public Health and Environment), because both doc-

tors and the public are now more aware of Q fever. As a consequence, more blood samples of people with symptoms such as fever, coughs and headaches are being sent to the lab for analysis. It is probable that many people were infected with Q fever in the past, but that most of them hardly noticed it. This is because more than half of the people infected with Q fever show no clinical symptoms. At the other end of the spectrum, a tiny percentage of those infected suffer chronic symptoms over many years.