

Conference on Q-fever 25-26.2.2010

The conference organised by the Ministry of Agriculture in collaboration with Wageningen UR and the Animal Health Service started early on Thursday 25 February.

25 February

The first day was chaired by **Jaap Wagenaar** (Veterinary Faculty Utrecht) with the opening words of welcome by **Elske Smith** (Ministry LNV/Agriculture). Wagenaar emphasised that the conference had an informative character and that therefore, the audience was supposed not to ask any political questions.

Christianne Brusckhe (Ministry-CVO) – *Actual veterinary situation and developments in the Netherlands*

Christianne sketched the development of the Dutch situation from the veterinary point of view. The human side of the problems would be outlined in the next presentation by Yvonne.

No one in the Netherlands had ever expected that after the first human cases (2007) this epidemic would grow to such proportions. Nowhere in the world has such a development been documented before.

At this moment 70% of all dairy goat farms is still Q-fever free. Some contaminations were caused by transporting animals from one farm to the other.

Investigations into an industrial way of killing the bacterium in manure are in process. Much is still to be learned about the Dutch problem.

Yvonne van Duynhoven (RIVM) – *The story of human Q-fever in the Netherlands*

There have been retrospective investigations into previous clusters of Q-fever patients in hospitals: 2 in 2005, 1 in 2006 and 4 in 2007.

In Herpen (first village in Brabant reporting human Q-fever) 24% of the people became infected.

In Helmond: 30% abortions in a goat farm resulted in the first human cases 3 weeks later. Most of them in the 2km-zone and decreasingly in the 5km-zone.

Research into the risks of an infection for pregnant women showed no complications for partus or newly borns.

The Public Health Council has been requested to advise on the possible use of a human vaccine. Answer in June.

Diagnostic delay has decreased: more awareness made patients visit the doctors sooner and the doctors did not wait long before checking for Q-fever.

How come that in all Q-fever literature just 5 % serious illness is mentioned, when in the Netherlands 20% is hospitalised? An artefact?

The hospitalisation rate has gone down from 20 % to 16.8 %.

Occurring complications: hepatitis 3.5% and endocarditis 0.3 %.

Francisco Reviriego Gordejo (DGSANCO) – Q-fever: the EU public and animal health legislative context

Riviriego sketched us how Q-fever is apparently an underestimated and under-listed disease. Not included in EU legislation for animal diseases in contrast to Brucellosis and RVF; and as a zoonosis not explicitly listed in zoonoses- monitoring in contrast to Brucellosis and Salmonella. Q-fever is progressively covered by EU surveillance for PH- monitoring. In the basic OIE standards Q-fever is listed but not for international trade.

Apparently the EU wheels are turning slowly, however moves are being made now to include Q-fever in future as a notifiable disease.

Pia Mäkelä (EFSA) – Current reporting and monitoring of Q-fever in animals in EU

EFSA collects yearly data on monitoring of zoonoses. MSs have to submit these data on 8 zoonoses, among which Q-fever is not listed. However based on the epidemiological situation of the MSs other zoonoses may be included. Currently data of 7 other zoonoses, among which Q-fever, are reported. EFSA collaborates closely with ECDC (European Centre for Disease prevention and Control) to analyse and publish the yearly reports. Reporting list B diseases (like Q-fever) or not is an MS decision. Encouraged by EFSA Q-fever reporting started in 2005. Since then more and more MSs are sending in their data. The reported data are not harmonised: most reports are from clinical investigations (abortions), some from monitoring, some from surveillance and some from surveys. Data do not show whether they are herd based or from individual sampling, nor what diagnostic methods were used. So data between MSs are not comparable. EFSA has given a grant to a consortium of MSs' institutes (AFSSA/France, CVI/Netherlands, FLI/Germany and NVRI/Poland) led by AFSSA: to produce a harmonised monitoring and reporting scheme for Q-fever in animals. (See Richard Thiéry's presentation on 26 February). Up till today Q-fever was present in all 18 reporting MSs. Without harmonisation it is impossible to interpret the data.

Denis Coulombier (ECDC) – Implications for public health in the EU

ECDC is involved in an advisory role re Q-fever since 2007/08. With the rise of cases in the Netherlands there seems to be a new dimension in the Q-fever situation. The EU Commission has requested ECDC to assess the risks. The Bavarian problems in Germany appear to be not related to the Dutch situation.

His conclusion: Confirmed circulation of *C. burnetii* should start early warning for public health.

Jeannette van de Ven (ZLTO) – The meaning and consequences of Q-fever for farmers in general and especially the situation of goat farming

Jeanette and her husband started the family farm in 1995 with 200 lambs and have expanded that number to 2000 goats today. In 2008 their farm is situated in the compulsory vaccination zone, and therefore all animals were vaccinated twice (boost after 6 weeks); in 2009 the old animals were vaccinated once and the lambs twice. Then in December 2009 the farm was declared contaminated based on bulk milk monitoring → of 2000 animals 524 pregnant animals were killed in the first round and 101 in the second.

Not only did she tell her own sad story, she also told us about a farm outside the compulsory vaccination zone where all animals had been vaccinated voluntarily and yet this farm too was

declared contaminated. Again the pregnant animals were culled based on bulk milk testing results. Bulk milk tests give no information about the number of infected animals at a contaminated farm. It could be that the majority of culled animals was healthy. At the moment there is continuing uncertainty for the farmers: the breeding ban is set till July 2010, but what is going to happen afterwards? The culling policy undermined the vaccination policy. The vaccination policy should have avoided unnecessary killing as control policy. Farmers are eager to do everything to prevent people from getting sick (therefore they did agree to the drastic measures this time), but eradication of the bacterium is impossible. There must be a risk based balance in future and not a policy based on sentiment and media impact.

Annie Rodolakis (France) – *Q-fever in France*

An elaborate description of the Q-fever situation in France where most human cases were due to infection in sheep herds. To compare virulence of strains a mouse model was developed. Sheep strains appeared to be less virulent for mice than the ones from bovines and goats. So possibly other factors could be responsible for the route to humans. Sheep mostly shed in faeces and vaginal mucus. Bovines hardly do.

Studies into the efficacy of the available vaccines showed that the CEVA vaccine Coxevac is very efficient, not only reduces the number of abortions in a herd but also the amount of shedding. Whereas the Merial vaccine Chlamyvax (combination vaccination against *Chlamydia* and Q-fever) did neither.

The French have developed a skin test for infected herds to determine which ones are to be vaccinated. Then one can suffice with vaccinating the ones with negative reaction. Hygienic measures are in place as well, like carefully destroying after birth material (so it will not be eaten by domestic or wild animals), births in confined locations, disinfection of these locations afterwards and treating the manure with lime or calcium cyanamide and later not spread it in windy conditions. Still more research is done regarding the best way to handle manure and the other hygienic measures.

Stephen Graves (Australia) – *Epidemiology and the role of human vaccination*

After giving us the history of *C. burnetii*, Graves told us that Q-fever is widely spread in Australia, with concentrations in Queensland and anywhere around localities with livestock and abattoirs etc. Australia is an empty country with widely scattered farms (lots of space for all the Dutch goats). The *Coxiella* bacterium is found in all ruminants, kangaroos and the kangaroo tick. Not so much in domestic animals. Most human cases are due to aerosol spread from dried animal waste. The Australians developed a vaccine for humans, licensed in 1989. It is still the only approved human vaccine in the world. However before vaccinating a person one MUST (obligatory) perform a skin test to prevent nasty reactions from the vaccine. Anyone with previous Q-fever history will test positive and therefore be excluded from vaccination, unless the risk of infection is higher than a possibly nasty reaction to the vaccine. Vaccination is supposed to last 10 years.

Q-fever (for humans) is a notifiable disease. It is often not diagnosed, therefore under-diagnosed. The incidence is higher in dry years.

Vaccination is not government funded; however meat-related companies take responsibility by offering their workers vaccination, although economic reasons to diminish workers' absence play a

role as well. The use of vaccination in rural communities is common.

His suggestions for the Netherlands:

“Buy our vaccine, try its efficacy for your local strains and then develop your own vaccine. Good luck!”

Martin Ganter (Germany) – *Q-fever in Germany*

In Germany there have been over the years (notifiable since 1947) some outbreaks of human Q-fever. Mainly in the south (Bavaria). But there have been two outbreaks in Jena/Thuringia (2005) and in North Rhine-Westphalia¹ where in 2003 some 300 people became ill with Q-fever after they had visited a country fair. There one aborting sheep had shed *C. burnetii*). In the Jena valley a small flock of sheep lambing was the cause.

[By the way, if I am informed correctly the farmers there voluntarily chose to kill the flock.]

There are no specific regulations for Q-fever; it is handled when necessary usually by the veterinary officer, who can instate a transport ban, hygienic measures regarding birthing and disposal of material; and antibiotic treatments (tetracyclines) and vaccination. But all this depends on the available knowledge of Q-fever of the involved persons. Due to some large outbreaks a research network of human and veterinary groups is working on diagnostics and epidemiology of Q-fever. Ganter has performed his own trial (ongoing) to research and evaluate the vaccination of a pregnant flock of sheep. It looks like there is a decrease (in 2009) of *C. burnetii* in the flock, but too soon for conclusions.

Paula Menzies (Canada) – *Q-fever & Coxiellosis in Canada*

Canada is an empty country. However in Ontario there are high animal concentrations (sheep and goats). Reported human Q-fever (notifiable) cases are low. Coxiellosis (Q-fever) is not reportable for animals, but annually notifiable. No actions are taken after diagnosis. No routine surveillance. Outbreaks (human) are always related to visiting barn shows and fairs. No human cases reported due to cattle; there are links with cats and trapping hares (wildlife). After cod fishery collapsed Newfoundland imported goats to start dairy goat farming. In the ‘virgin’ area the *Coxiella* found a nice host. Several outbreaks: on 6 of the 8 farms. Poor Newfoundland had imported the devil. However Coxiellosis is unlikely to become reportable in Canada, and is under-diagnosed in general. Better communication to the public is needed. More awareness with the authorities is needed. And Menzies is seeking support in the Netherlands for her efforts towards the Canadian government. In May this year a study starts on prevalence in Ontario. Suggestions are welcome!

General discussion and final remarks/closure

It seemed that most questions were asked and Wagenaar concluded that the speakers had made us a lot wiser and given many answers to our questions.

¹ Both cases are described in this article: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1618839>

26 February

Chairman: **Frits Plumers** (former Ministry CVO)

Benaouda Kadra (CEVA) – *Q-fever: Vaccine production and control*

As producer of the vaccine Coxevac Kadra gave us an overview of its benefits and of the production process (purification of the virus is a difficult technique). Coxevac is registered in France since 2004 and is used on a voluntary basis. The Netherlands have a temporary authorisation since 2008. The Dutch have bought every possible available dose for 2010. Because of the difficult production process there will be not one extra dose this year.

Hendrik-Jan Roest (CVI) – *Diagnosis, genotyping, virulence and culture of C. burnetii in the Netherlands*

In the Netherlands bulk milk testing is used since October 2009; before that the abortion rate of >5% was the indicator to notify. A lot of discussion has been going on about the efficiency and credibility of bulk milk testing as a criterion for culling. However according to Roest the detection of *C. burnetii* in a milk sample gives an absolute positive result, even if another test should be negative. And the fact that at culled farms the last test results were negative after positive initial results does not mean there is no infection on the farm only that the shedding went below the detection line. 30% of the animals will not be detected → false-negatives.

In genotyping 13 types were found in the Netherlands, using Multi Locus variable number tandem repeat Analysis (MLVA). MLVA-type 11 is predominant on all Brabant farms and on all dairy goat farms. Harmonising of the typing methods is essential for interpretation (see EFSA-grant). Whether the predominant type 11 is more virulent than the others is still a question not answered. However in cooperation with France some Dutch and some French strains will be compared to find the answer, expectedly this year. We have to consider as well that the Dutch goats and people are relatively virgin regarding Q-fever, so therefore the effects could possibly be worse.

Richard Thiéry (AFSSA) – *Results of EFSA's grant on improving harmonised Q-fever monitoring in the EU*

As we heard from Pia Mäkelä (EFSA) reports from MSs are not harmonised and can therefore not be interpreted or compared. The EFSA-grant to AFSSA (in collaboration with CVI, FLI and NVRI)² aims to create a harmonising-system. So harmonisation is the key-word. In 14 of 18 reporting MSs the disease is notifiable for animals. Some MSs are reporting at level of animals (individual) others at herd level. There are f.i. no definitions or specificity of clinical signs. Harmonisation will start with central reporting of: clinically affected herds (of domestic ruminants only) after serial abortions and presence of the bacterium is confirmed by PCR, and positive serology by ELISA. RT-PCR is most effective when performed within 8 days after abortion and ELISA is very effective in vaccinated herds. For active surveillance bulk milk testing is very effective. The final report is expected this spring.

² Afssa – Agence Française de Sécurité Sanitaire des Aliments; CVI – Central Veterinary Institute (NL); FLI – Friedrich Loeffler Institute (DE); NVRI – Nat. Veterinary Research Institute (PL)

Dimitrios Frangoulidis (Germany) – *Coxiella burnetii* - stability in the environment and molecular typing

There are 55 strains and 17 genotypes. Despite the fact that *C. burnetii* is spread all over the world, is found in many species and has outbreaks all over the world, it is rarely reported. *C. burnetii* is known as large cell variants (LCV) and small cell variants (SCV). The small variant is more stable and can survive in soil or dust for many years, and survive in many circumstances like in acids and high temperatures (70 degrees for 15 minutes). Diagnostic capabilities have improved over the years, but there is still a lot to be learned about the epidemiology of the disease.

Piet Vellema (Animal Health Service Deventer) – *Research in relation to the approach of Q-fever*
Bulk milk testing was initially (October 2009) aiming at accrediting repeatedly test negative dairy farms. However in December 2009 this testing was used to identify positive farms and consequently kill all pregnant animals at such farms.

Efficacy of vaccination was tested on 15 dairy farms. There was some raise of temperature, some skin effects, and a few cases of milk production reduction. However the shedding of bacteria was considerable after some time. (see presentation)

At the request of the audience (questions to previous speakers) Vellema elaborated on research into the relation between temperature in the manure heap and survival of the bacterium. It became apparent that the temperature in manure rose to 70+ degrees within two days, but only in the upper layer. The core never rose above 40 degrees. The more oxygen could be induced (like in the top layer) the higher the temperature rose. As up-turning a contaminated heap produces the risk of freeing bacteria, one believes that airing the heap with pipes would be the best way to raise the temperature in the core.

End of a very interesting and well organised conference with a wide range of speakers, enough time for questions and discussion.

In the afternoon the speakers and invited experts and stakeholders remained to discuss several angles in smaller groups. This session was open only to the selected people.

This conference was attended and the report made by Christine Bijl, as ELA representative.

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