The Schmallenberg virus

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In a matter of months, a new virus has succeeded in infecting a large majority of ruminants in Europe. While not particularly worrying in adult animals, the clinical signs in foetuses infected during gestation are, however, alarming: abortion, hydrocephalus, muscular atrophy. A team from the University of Liège’s Pathology Laboratory is closely monitoring this new epidemic.

In autumn 2011, breeders and vets in the eastern part of the Netherlands and the west of Germany discovered the first clinical signs of a new epizootic. The symptoms in their cows, sheep and goats were fever, diarrhoea and a drop in milk production. These symptoms very quickly affected a large number of animals on the same farm and as it was identified in numerous farms in a given geographic region, the situation began to resemble the start of a new epidemic. Hence, the next step was to find and understand the nature of the disease to be able to estimate the seriousness of the situation and get it under control as quickly as possible. While the clinical signs in adult ruminants aren’t alarming, those present in foetuses infected during gestation are significantly more striking. "The symptoms observed in adult animals aren’t very specific and only last about a week. On the other hand, this new pathogen can cause abortions and serious malformations, especially in the nervous system of young animals infected during gestation", explains Mutien-Marie Garigliany, doctor in veterinary medicine and research assistant at ULg’s Pathology Laboratory, led by Professor Daniel Desmecht.

A new hybrid virus

Researchers at the Friedrich Loeffler Institute (FLI), the main federal German research organisation for animal health, were therefore quick to begin looking for the causes of this epidemic. Since the traditional analyses didn't provide any results, the scientists launched a metagenomic study. "This consists of randomly amplifying all the pieces of RNA and DNA contained in the samples taken from animals affected by the disease"
and then sequencing them all", explains Mutien-Marie Garigliany. By amplifying all the genetic material in this way, the researchers came across many things of little interest, such as pieces of the genome of the sick animals or genetic material belonging to traditional pathogens found in ruminants. "But they also spotted an Orthobunyavirus-like viral genome similar to the Shamanda virus and they wondered whether this was the source of the problem", the researcher from Liège points out. On the basis of the first sequences obtained, the FLI team created an initial PCR (polymerase chain reaction) and realised that all the samples from the animals showing clinical signs contained genetic material from this virus!

Once this initial observation had been established, the German scientists analysed the pieces of the viral genome more closely. It was then that they discovered that the pathogen in question wasn’t the Shamona virus but a new one. "Like the flu virus, this new virus is composed of several genomic segments", Mutien-Marie Garigliany emphasises. "The Schmallenberg virus, named after the German town where the first cases were discovered, contains three genomic segments, two of which come from the Shamond virus and one from the Sathuperi virus", he continues. Well known and identified quite some time ago already, first in Africa then in Asia, these two viruses are relatively inoffensive. "The specific combination of the genomic segments as found in the Schmallenberg virus cause a virulence that isn’t observed in the ‘parent’ viruses", the researcher points out.

Nerve cells in the firing line

Just like the virus responsible for bluetongue disease (BTV) (see article The fight against bluetongue disease), the Schmallenberg virus is transmitted from one animal to another through a vector: culicoides. In fact, researchers at University College London have shown that some of these midges are carriers of the new virus, especially in the samples of culicoides collected in autumn 2011... "What's extraordinary", Mutien-Marie Garigliany continues, "is that while having a very short viremia this virus has managed to infect a large majority of ruminants in Europe. This raises questions", he stresses. "Are there perhaps other means of transmitting this virus? Several teams are currently studying this hypothesis", the researcher continues. The vector isn’t the only point in common between the bluetongue virus and the Schmallenberg virus. Indeed, like its predecessor, the latter can cause nerve lesions in infected foetuses. "If the infection occurs during a certain window of the gestation period, sufficiently late so that the placenta is in place and sufficiently early in the development of the foetus, the virus can affect certain tissues and cause malformations", explains Mutien-Marie Garigliany.

Among other things, the Schmallenberg virus attacks nerve cells leading to their gradual destruction. The symptoms vary depending on the stage of development during which the foetus was infected. The earlier the foetus comes into contact with the virus during its development, the greater the risk of abortion because the malformations caused aren’t compatible with the foetus' survival. However, in the majority of cases, the young are born at term or slightly early and mainly have abnormalities in the encephalon, especially hydrocephalus. "Basically, the encephalon is comprised of ventricles, which are cavities containing cerebrospinal fluid, and a cortex of nerve tissue", the scientist tells us. "Normally, the cortex is thick and the ventricles are small, but in the case of hydrocephalus, these proportions are reversed. The ventricles take up a lot of space and, in extreme cases, the cortex becomes nothing more than a fine membrane of nerve tissue. This is referred to as hydranencephaly".
Study of an atypical case

Mid-January 2012, Professor Daniel Desmecht, Mutien-Marie Garigliany and Calixte Bayrou, assistant in the Pathology Laboratory, were entrusted with a somewhat atypical case. "We had the chance to be able to study a living and viable calf despite the almost total absence of an encephalon", reveals Mutien-Marie Garigliany. "This allowed us to observe the nerve signals associated with brain lesions in a living animal". The animal was then euthanized for ethical reasons. "We carried out tests to ensure the presence of the Schmallenberg virus in the lesions as well as tests allowing us to exclude the involvement of other viruses", the researcher specifies. This work was published in the journal *Emerging Infectious Diseases* in June(1).

The autopsy room at the Faculty of Veterinary Medicine at ULg is renowned in Europe, especially for the large number of bovine autopsies carried out there. Owing to its reputation, the ULg Pathology Laboratory team received a great many calves with clinical signs characteristic of infection by the Schmallenberg virus. "In pathology, we study lesions in individuals after death, first on a macroscopic level and then on a microscopic level", explains Mutien-Marie Garigliany. "We systematically took samples from many different organs such as muscles, internal organs, skin, etc. And we're in the process of making a detailed study of the organs affected by the Schmallenberg virus". While the lesions are most spectacular in the encephalon, infected newborns have other abnormalities such as muscular atrophy. "Discovering the organs infected by this virus will help us to understand its biology, which seems to be relatively complex", continues the researcher.
Nine cattle out of ten infected in Belgium

Finally, Mutien-Marie Garigliany and his colleagues have also undertaken serological studies whose results will also be published in the Emerging Infectious Diseases journal (2). One study aims to analyse, on a large scale, the percentage of cows with antibodies against the Schmallenberg virus, which have therefore already been infected by it. The other aims to detect the presence of antibodies against the same virus in calves that haven't yet ingested any colostrum. "Colostrum is the first maternal milk every mammal drinks. Among other things, it contains antibodies from the mother. So, if calves who haven't drunk this milk have antibodies against the Schmallenberg virus, these antibodies can only result from the calf's immune response in utero", the researcher stresses.

As regards the first serological study, the researchers demonstrated, among other things, that 90% of adult cattle in Belgium are seropositive for the Schmallenberg virus. "We therefore know that a large majority of cattle were infected with the virus at the end of last year", Mutien-Marie Garigliany continues. As for the serological study relating to calves, the results show, among other things, that 30% of clinically healthy calves have antibodies against the new virus before ingestion of the colostrum. "These calves have probably been infected in utero late in the gestation period and the virus was thus unable to interfere with their development", explains the specialist.
The researchers from Liège have published an article in the *Antiviral Research journal* (3) that includes the clinical, pathological, virological and epidemiological facts made public during the first six months of the emergence of the Schmallenberg virus.

**A new wave of infection expected in spring-summer 2012**

It is difficult to give an exact figure for the number of farms affected by this new epidemic in Europe since it is continuing to evolve, but we are talking about more than 3 500 cattle farms affected, including sheep, goats and cattle. "The vector needs humid and relatively warm places, such as barns, to survive. But the colder periods this winter prevented the circulation of the culicoides during the last months", Mutien-Marie Garigliany points out. So while the epidemic may have gone through a quiet period over the winter, a new wave of infection is expected, but probably to a lesser extent, with the arrival of fine weather and new calves.

As regards the evolution of the epidemic in the coming months, it would appear that the worst of the storm has passed. "It's likely that some adult animals will still have clinical signs and that some young ruminants will be born with malformations during the next season, but that should then stop for several years at least", the researcher continues. "The majority of animals will have been infected and once the mothers have a high level of antibodies in their blood, which is the case in 70 to 90% of cattle in Europe, this will have a neutralising effect and prevent the virus from passing through the placental barrier", Mutien-Marie Garigliany adds. Hence, the Schmallenberg virus should soon no longer be able to cause too much damage.

In the longer term, European cattle may however become gradually naive - i.e. seronegative for the Schmallenberg virus - or quite simply, the whole herd may be renewed in the next five to six years and then there may be a new epidemic.

**No health risks for humans**

While the idea of developing a vaccine for ruminants against the Schmallenberg virus was mentioned at the beginning of the epidemic, this was quite quickly abandoned because by the time the vaccine reaches the market, 100% of ruminants will have been infected by the virus and will be immunised.

As for the risks on human health, there don't appear to be any. "*The virus doesn't cause any clinical signs in man. Better still, humans don't seroconvert, i.e. they don't produce antibodies, even after close contact with sick animals. This shows that the Schmallenberg virus is incapable of infecting man*", explains Mutien-Marie Garigliany. "*We have also done tests on mice and we obtained an identical result. Clearly, there is a species barrier*".

The Pathology Laboratory team is currently continuing its research on the biology of the Schmallenberg virus and is attempting, among other things, to find out more about what prevents this virus from crossing the species barrier. "*We are examining whether this could change because the consequences of this virus infecting humans could be dramatic*", the scientist concludes.

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