RAG-V-EZ
RISK ASSESSMENT GROUP
VETERINARY – EMERGING ZOONOSES

Risk assessment and recommendations for Belgium with regards to infections in cattle and goats with highly pathogenic avian influenza A(H5N1) clade 2.3.4.4b virus in the USA

11/04/2024

This note is developed in response to the recent events of cattle and goat infections with HPAIv A(H5N1) in the USA. It is addressed to authorities and to the RAG/RMG. It contains an assessment of the risk for both animal and public health associated to ruminant infection with **HPAIv A(H5N1)** in the Belgian context. Recommendations for actions are given to better assess the exposure of the Belgian cattle/goats to HPAIv A(H5N1) and the risks related to this.

1. State of the art concerning scientific and epidemiological knowledge on Influenza A infection in cattle and goats

Based on previous knowledge, **Influenza A virus (IAV) infection occurred very rarely in the *Bovidae* family**. Hence *bovinae/caprinae* have not commonly been considered as highly susceptible hosts for IAV.

The scarce literature data inform on:

(i) previous natural cases of IAV in cattle. These cases were rare and only punctually confirmed by successful virus isolation, confirming bovine as low susceptible species;
(ii) seroprevalence studies of IAV infection in cattle, very often without clinical signs in the sampled animals;
(iii) successful experimental IAV infection in cattle but with very low shedding.

These data are summarized in Sreenivasan et al., 2019.

2. Scientific and epidemiological knowledge about Influenza A(H5N1) clade 2.3.4.4b infections in cattle and goats in the USA

In March 2024, HPAI A(H5N1) was reported in 10 neonatal goat kids. They were displaying neurological signs and mortality, in agreement with a 'classical' clinical picture of HPAI infections in mammals. These goat kids had contact with infected captive birds. The Eurasian lineage goose/Guangdong (Gs/Gd) clade 2.3.4.4b. was detected (Minnesota Board of Animal Health).

Next to this, cases of HPAI A(H5N1) infections in cattle have been reported in several American states (Kansas, Texas, Michigan, New Mexico, Idaho, Ohio and North Carolina) (USDA). The clinical signs in cattle included atypical mastitis with drop in milk production and thickened or colostrum-like milk, loss of appetite, changes in feces consistency and low-grade fever. These clinical signs are rather untypical for HPAI infections in mammals and, together with mastitis and virus detection in raw milk, may suggest an infection of the mammary gland. Unpasteurized milk and oropharyngeal swabs of these cases tested positive for HPAI A(H5) viruses of the genetic Eurasian lineage Gs/Gd clade 2.3.4.4b.

It is important to notice that the HPAI A(H5N1) strains now circulating in the USA are genetically diverging from the European HPAI A(H5N1) circulating strains probably due to both natural genetic evolution and reassortment between the originating strain and local avian LPAI strains.

From an epidemiological point of view the goat and the cattle outbreaks must probably be assessed separately as the clinical picture between goats and cattle differ, probably due to different routes of infection:

- the cases in goat kids, displaying usual clinical signs of mammal infection by HPAI virus and were in close contact with infected captive birds; while
- the cases in cattle have been associated with drop in milk production, atypical mastitis, virus detection in milk and any severely depressed animals without both respiratory or neurological signs. Environmental infection of the udder could be suspected, e.g. during the milking process. Cattle-to-cattle transmission has also been suspected based on circumstantial evidence. Yet this has not yet been confirmed and the geographical spread could also be due to movements of infected animal from a primary outbreak as observed for other influenza virus.

One isolated human case of infection is currently associated to these cattle infections. This human case was in close contact with the animals. Therefore, cattle-to-human transmission is also suspected. The symptoms observed in this human case were not severe (conjunctivitis). Epidemiological investigation is still ongoing. One of the genetic mutation known to make the virus more transmissible to mammals has been shown in the human isolate (PB2-E627K; M. Steensels, personal communication).

Update information on HPAI detections in livestock as well as biosecurity recommendations and other resources can be found on the webpage of the Animal and Plant Health Inspection Service (APHIS) of the USA.

The **following unknowns** about cattle and goats infections in the USA remain : (i) the initial route of infection for cattle in particular if they can be infected via the respiratory route and/or the digestive route and/or another route associated to environmental contamination, (ii) the viremic status of the animals, (iii) the duration for virus shedding and (iv) the related excretion routes in cattle (i.e. ability to excrete infectious virus via the respiratory route and/or via the feces and/or milk), (v) the transmissibility between cattle (i.e. if cattle-to-cattle transmission occurs) as well as to human, and (vi) the potential infectivity of raw milk or dairy products containing raw milk.

3. Belgian cattle exposure

With the wide spread of the HPAIV A(H5N1) clade 2.3.4.4b strains in wild birds, mammals are more exposed to IAV than before. In the Belgian epidemiological context it is considered that, **the main sources of infection for cattle/goats remain direct or indirect contacts with infected birds**.

Since the beginning of 2024 (from 01/01/2024 to 28/03/2024), 2 cases in wild birds have been reported in Belgium by Sciensano (but the cadaver reporting efforts in the wild might be reduced due to the ongoing duration of the epidemic). Yet throughout Europe a limited number of new cases of HPAIV in birds and poultry are reported suggesting that the infection pressure on cattle/goats can currently be considered as low.

Wild mammals must be considered as another potential source of cattle exposure. Cases of mammal-to-mammal infection have been suspected both in captive and wild mammals. Yet, up to now, none of these has been confirmed.

There is currently no monitoring or surveillance system in place in cattle in Belgium or other European countries with comparable cattle production sectors to provide accurate data on the likelihood of (sub-clinical) infection with HPAIV of the cattle population.

The **likelihood of exposure of cattle and goats** to HPAIV (H5N1) clade 2.3.4.4b in the current condition is assessed **as 'very low'** in Belgium. Considering the ever changing situation and the many uncertainties and unknows, **continuous reassessment** of the likelihood of exposure remains necessary to assess the risk and correctly inform the risk managers.

4. Public Health consequences and considerations on raw milk and dairy products made with raw milk

The review by Sreenivasan indicates that cross-species transmission previously occurred at the human/cattle interface, but scarcely. So, cattle-to-human transmission cannot be excluded. This is also in line with the observed human case in a cattle farm in the USA. Until today, no human case of infection with HPAI A(H5N1) clade 2.3.4.4b has been described in Belgium. Even if zoonotic transmission from mammals cannot be excluded, it remains a rare event with the current HPAI A(H5N1) strains. Uncertainties remain high regarding the possibility of transmission via consumption of raw milk and products thereof from infected cattle.

In the USA, recommendations have been made to not manufacture or sell raw milk or raw/unpasteurized milk cheese products made with milk from symptomatic cows and those exposed to HPAIv. Consumption of pasteurized (i.e. pasteurized or sterilized or UHT treated) milk or milk products is considered to be safe.

Indeed, pasteurization fully eliminates the infectivity of influenza virus in milk (eCDC). **Therefore, there is no risk of consuming pasteurized milk or dairy product made with pasteurized milk**. **Milk from diseased animals is not authorized in the food chain**.

5. Qualitative risk assessment in the Belgian epidemiological context (dd 11 april 2024) and conclusions

To date, HPAI has not been reported in cattle neither in Belgium nor in the EU/EEA. Based on the current available literature and information as well as the epidemiological context, the RAG-V-EZ is currently assessing the **risk[1] of infection of cattle/goats with HPAI A(H5N1) as 'very low to low'**. This assessment should be confirmed by field data, e.g. via a monitoring on a representative fraction of the cattle and goat population in Belgium.

This risk assessment is in line with the current risk assessment by WHO and eCDC for zoonotic infection and Public Health: 'low' for the general population in the EU/EEA and 'low to moderate' for occupationally or otherwise exposed people to infected birds or mammals (wild or

[1] The risk is here considered as the result of the likelihood of exposure of cattle to HPAIV (see above) and the consequences thereof in the Belgian epidemiological context.

domesticated). **Moreover, pasteurized (i.e. pasteurized, sterilized or UHT treated) milk and dairy product made from pasteurized milk are safe**.

Several uncertainties remain from the situation in the USA which will need to be closely followed. Continuous update of this risk assessment will be needed depending on further information.

6. Recommendations

- In order to assure a rapid detection of infections it is advisable to develop clear communication to **Increase the awareness** among farmers as well as veterinarians on the possibility of HPAIV infections in cattle and goat and the accompanying clinical symptoms such as atypical mastitis, drop in milk production, reduce appetite, thickened/discolored milk, lethargy, fever, and/or dehydration, respiratory/neurological signs. Such a communication campaign could be initiated by the FASFC in collaboration with its laboratory and academic partners.

- To assess the presence of the HPAIV in the cattle or goat population in Belgium **a retrospective evaluation of historical serum and/or milk samples should be executed**. This is preferably done on samples from the most exposed farms (by example those located in sensitive areas for HPAI or where most of the infected wild birds have been found). This retrospective analysis could be performed by the reference laboratory in collaboration with the regional animal health services. Depending on the results of this evaluation, further scenarios on monitoring programs as well as recommendations on testing and risk mitigation can be developed.

- To facilitate detection of HPAIv infections in cattle **it should be included in the differential diagnostic of cattle/goats with respiratory signs, milk drop, mastitis and neurological disorders,** in particular for those with increased exposure to infected birds. Tests should be carried out either on milk samples (possible for lactating cattle/goats) or on nasal swabs (for both lactating and non-lactating cattle/goats with respiratory signs). Milk sampling is the easiest sampling method for serology at herd level, and nasal or tracheal swabbing/bronchoalveolar wash is the most sensitive test for virus detection in individuals. This can be considered within the awareness and communication campaign. Laboratories should develop the necessary test capacity;

- For a better understanding of the risks **further research** is needed on the pathogenesis of HPAIv infection (European strains) in ruminants or on derived cells thereof, including for the mammary gland. Also the persistence of the infectivity in raw milk and in dairy products based on raw milk should be studied;

- To reduce the risk of HPAIV infections in cattle it is advised to **assure good biosecurity practices and inform farmers/vets on this:** this includes the reduction of contact between cattle and wild birds, poultry or other animals that may carry HPAIv; avoid housing multiple species of animals in close proximity; isolate cattle with clinical signs from the rest of the herd as soon as possible; do not use manure from poultry on pastures for cattle, the removal of dead wild birds from pastures. Increased communication on good biosecurity in cattle and goat production could be performed by the regional animal health services and specialized biosecurity organizations;

- To reduce the risk of infections in humans **the public should be informed on the risks associated with consumption of raw milk and dairy products based on raw milk** (not only HPAIv). At the same time the message should be distributed that it is safe to consume pasteurized milk and milk

products. Such a communication could be initiated by the FASFC in collaboration with the federal public service Health, food chain safety and environment.

7. References

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