Listeria monocytogenes infection in ruminants: Is there a link to the environment, food and human health? A review

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Summary

Listeria (L.) monocytogenes is widely distributed in the environment, but also has the ability to cause serious invasive disease in ruminants and humans. This review provides an overview of listeriosis in ruminants and discusses our insufficient understanding of reservoirs and possible cycling of *L. monocytogenes* between animal and human hosts, food and the environment. It indicates gaps in our knowledge of the role of genetic subtypes in *L. monocytogenes* ecology and virulence as well as risk factors, *in vivo* diagnostics and pathogenesis of listeriosis in ruminants. Filling these gaps will contribute to improving the control of *L. monocytogenes* and enhancing disease prevention. As the prevalence of listeriosis in ruminants in Switzerland is likely to be underestimated, propositions concerning improvement options for surveillance of listeriosis in ruminants are provided.

Keywords: listeriosis, subtypes, ecology, virulence, surveillance

Listeria monocytogenes Infektion bei Wiederkäuern: Besteht eine Verbindung zur Kontamination von Umwelt und Lebensmitteln und zur menschlichen Gesundheit? Eine Übersicht

Listeria (L.) monocytogenes ist ein weit verbreiteter Umweltkeim, kann jedoch im Falle einer Infektion eine schwere invasive Erkrankung bei Mensch und Wiederkäuer hervorrufen. Dieser Artikel gibt eine Übersicht über die Listeriose beim Wiederkäuer und diskutiert gegenwärtige Wissenslücken bezüglich Reservoirs von *L. monocytogenes* und dessen mögliche Übertragung zwischen Tier, Mensch, Lebensmittel und der Umwelt. Die Rolle von genetischen Subtypen in der Ökologie und Virulenz von *L. monocytogenes* ist bisher nur wenig geklärt und die derzeitige Kenntnis von Risikofaktoren, *in vivo* Diagnostik und Pathogenese von *L. monocytogenes* bei Wiederkäuern ist ungenügend. Um die Kontrolle von *L. monocytogenes* im Sinne der Krankheitsprävention zu verbessern, wird es in Zukunft wichtig sein, diese Wissenslücken zu schliessen. Die angegebenen Verbesserungsvorschläge für die Krankheitsüberwachung haben zum Ziel, die Abschätzung der Prävalenz der Listeriose beim Wiederkäuer zu optimieren, da diese momentan mit hoher Wahrscheinlichkeit unterschätzt wird.

Schlüsselwörter: Listeriose, Subtypen, Ökologie, Virulenz, Überwachung

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Introduction

Listeria (L.) monocytogenes, a facultative intracellular pathogen, is able to cause serious invasive disease in animals and humans. It was first isolated from a human patient with meningitis in France in 1921 (Dumont and Cotoni, 1921) and thereafter from a wide range of mammalian and non-mammalian species worldwide (Murray et al., 1926; Low and Donachie, 1997). Although an association between listeriosis in animals and the ingestion of contaminated feed had already been suggested in the 1960s, it was not until the 1980s that *L. monocytogenes* was recognized as a causative agent of food-borne outbreaks in humans (Schlech et al., 1983). Since then, it has been associated with a wide range of different foodstuffs, including two types of Swiss soft cheese (Büla et al., 1995; McLauchlin, 1996; Bille et al., 2006). Compared to other food- and feed-borne infections, listeriosis is a relatively rare disease. Yet it is associated with an exceptionally high fatality rate, which is why its surveillance and control are a major public health concern. However, both are hampered by the wide distribution of *L. monocytogenes* in the environment, where the bacterium commonly lives as a saprophyte (Weis and Seeliger, 1975; Vivant et al., 2013). When ingested by humans or animals it is capable of turning into an intracellular pathogen (Freitag et al., 2009).

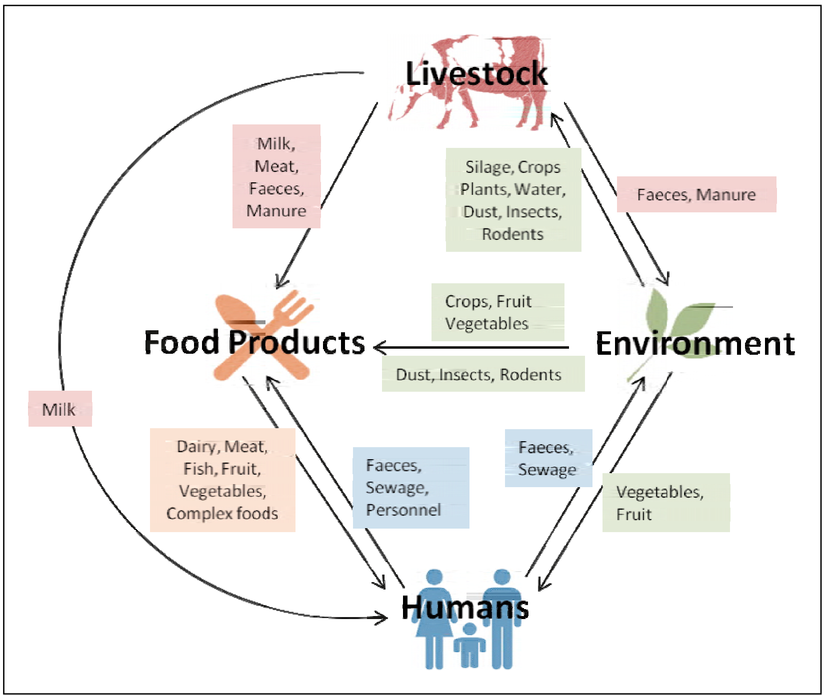

Figure 1: Transmission scenarios for *L. monocytogenes* between ruminants, humans, food products and the environment. Potential transmission pathways and vehicles are indicated by arrows and colored boxes, respectively.

L. monocytogenes is characterized by a high genetic diversity and comprises numerous strains, which have diversified into four evolutionary lineages (Ragon et al., 2008; Orsi et al., 2011). There are indications of inter-strain differences regarding virulence and transmission (Nightingale et al., 2004; Hain et al., 2007; Ragon et al., 2008). Serotyping was the first method developed for subtype discrimination of *L. monocytogenes* and has uncovered that the vast majority of human and animal infections are caused by only three different serotypes: 1/2a, 1/2b, and 4b (Okwumabua et al., 2005; Gianfranceschi et al., 2009; Lopez-Valladares et al., 2014;). These were also the most prevalent serotypes isolated from food and infected humans in Switzerland during the last decades (Pak et al., 2002; Bille, 2004; Althaus et al., 2014). However, serotyping has a low discriminatory power as it only allows to differentiate between 13 different serotypes. Accordingly, it has only limited value for epidemiological tracking, which is why in most countries high-resolution methods and, increasingly, whole genome sequencing of bacteria are applied for surveillance and outbreak investigation. It is currently not possible though to predict the virulence of a given isolate for men and ruminants based on its genotypic or phenotypic subtype. Consequently, there is a strong need to gather more information on strain-specific virulence by systematic correlation of genotypic/phenotypic strain data to the clinical context of isolation and to virulence data derived from infection models. Small-scale studies have been performed in several countries with an array of subtyping techniques (Sauders et al., 2004; Lyytikäinen et al., 2006; Gianfranceschi et al., 2009), making it difficult to compare data between studies. Therefore, the future strategy should focus on large-scale multi-laboratory studies applying a subtyping technique that allows sharing and exchanging data between laboratories. Furthermore, the identification of virulence genes and their variants that may be applied as markers either for disease-relevant strains or avirulent strains, respectively, is highly desirable.

Preventing the entry of *L. monocytogenes* into the food chain is challenging due to its ubiquity and high stress tolerance, allowing it to survive and persist under numerous environmental conditions (Freitag et al., 2009). However, it is still poorly understood how *L. monocytogenes* circulates between animals, humans and various environments (Fig. 1), and the question whether only specific *L. monocytogenes* subtypes find their way from the reservoir to the host remains to be fully addressed. Moreover, the determinants and mechanisms of transmission, in particular from the ruminant farm environment to humans, are not known at this point.

The purpose of this review is to provide an overview of listeriosis in ruminants and the occurrence of *L. mono-*

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cytogenes in livestock, humans, food and the environment. It aims at pointing out gaps in the current knowledge of the ecology of the pathogen as well as transmission pathways between its various niches and hosts. Furthermore, surveillance strategies for listeriosis in ruminants with particular regard to the situation in Switzerland are critically assessed.

Listeriosis in ruminants and humans

Clinical Presentation and Epidemiology

Clinical presentation of listeriosis is similar in all susceptible hosts and may include abortion, CNS infection or septicaemia. In veterinary medicine, listeriosis is of particular relevance to ruminants. It carries a high fatality rate and may present in 5 different clinical manifestations. Most common are encephalitides, followed by abortions in the last third of pregnancy (Wilesmith and Gitter, 1986). Other conditions like septicaemia in newborns as a consequence of *in utero* infection, mastitis and keratoconjunctivitis/uveitis occur less frequently. Subclinical infection is possible and may result in unnoticed pathogen spread by asymptomatic carriers (Ho et al., 2007). In consequence, faecal shedding of *L. monocytogenes* by seemingly healthy animals could pose a significant risk for contamination of animal feed, agricultural environments and raw produce (Ho et al., 2007).

In both humans and ruminants, infection with *L. monocytogenes* occurs predominantly due to consumption of contaminated feed and food. In ruminants, it has been linked in particular to the ingestion of poorly fermented silage (Gray, 1960; Wilesmith and Gitter, 1986). However, this association is being increasingly called into question due to the low number of systematic investigations on the one hand and diverging study results on the other. Faecal shedding of *L. monocytogenes* has been found to occur more frequently in animals that are fed with silage compared to other diets (Fenlon et al., 1996). Furthermore, a higher number of listeriosis cases and increased faecal shedding of *L. monocytogenes* has been observed during the colder months (Nightingale et al., 2005). However, the latter could also be explained by factors other than silage feeding, e.g. different husbandry types and an increased animal density during winter. At the same time, there is no evident link between listeriosis and silage feeding in up to a third of listeriosis cases and silage feeding did not emerge as a risk factor in a Swiss case-control study (Wiedmann et al., 1999; Spycher, 2012). It has also been shown that contamination of barn equipment like bedding, water and feeding troughs can be higher than in silage silos and bunkers (Mohammed et al., 2009). This raises the question whether there are other significant infection sources for ruminants apart from silage. Evidently, these sources require further characterisation. Systematic comparison of *L. monocytogenes* subtypes in clinically affected and unaffected ruminants and in the farm environment would significantly contribute to the identification of infections sources.

Listeriosis may occur as a large outbreak within a flock, but noteworthy, it is unlikely for different clinical manifestations to be observed during the same outbreak (Low and Donachie, 1997; Wilesmith and Gitter, 1986). This may indicate differences in organ or tissue tropism between *L. monocytogenes* strains. Most commonly however, few or single animals are affected (Low and Donachie, 1997). An unequal exposure of animals to *L. monocytogenes*, i.e. due to focal accumulation of *L. monocytogenes* in the feed or farm environment, could explain such a sporadic occurrence. Alternatively, infection of individuals may be facilitated by certain predisposing factors. While it is well established for humans that the elderly, pregnant women, newborns and immunocompromised patients are at particular risk for disease, individual risk factors for ruminants are still poorly understood. Such factors would include internal and external stressors and act by facilitating the host invasion or by weakening the host′s immune status, but have not been clearly identified yet (Wesley, 2007; Spycher, 2012). Second dentition acting as a portal of entry for *L. monocytogenes* has been implicated as a risk factor in ruminants (Barlow and McGorum, 1985). However, listeriosis frequently also affects adult ruminants with permanent teeth (Oevermann et al., 2010a). Gaining knowledge about risk factors of animal listeriosis is important in terms of disease prophylaxis and development of control measures to reduce animal disease. For this reason, it would be desirable to perform large-scale case-control studies to investigate the health status of affected animals and herds, farm management practices and their correlation with the prevalence of listeriosis cases and *L. monocytogenes* strains on the farm.

CNS infection

The CNS is frequently involved in both, animal and human cases, and accounts for the high mortality rate associated with listeriosis (Oevermann et al., 2010b). Most commonly, *Listeria* CNS infections in ruminants occur as rhombencephalitis, i.e. primarily affect the brainstem, and only exceptionally as meningitis or meningoencephalitis (Charlton and Garcia, 1977). This is in contrast to humans, where CNS infections most often manifest as diffuse meningitis and meningoencephalitis, and less commonly as rhombencephalitis or abscesses in the cerebrum and cerebellum (Mylonakis et al., 1998; Bartt, 2000). This discrepancy may be an indicator for a different pathogenesis in ruminants and humans. Today, listeriosis accounts for the majority of

CNS diseases in ruminants in many different countries (McGill and Wells, 1993; Agerholm et al., 2002; Miyashita et al., 2004; Oevermann et al., 2008; Iulini et al., 2012), but its prevalence in ruminant populations is likely to be underestimated for reasons outlined further below. High-resolution molecular subtyping methods indicate that listeric rhombencephalitis in ruminants is caused by particular neurotropic genotypes of *L. monocytogenes* (Pohl et al., 2006; Balandyté et al., 2011), but these results still need to be confirmed by screening of a larger number of strains and virulence studies. In addition, it remains unknown whether CNS infections in ruminants and humans are caused by identical strains. Identification of such particular neurotropic strains would enable targeted epidemiological investigations to study their distribution, ecology and potential to be transmitted to humans. Consequently, more specific measures for prevention and control of neurolisteriosis could be applied.

Pathogenesis of CNS infection

At present, the pathogenesis of neurolisteriosis is not entirely understood and importantly, the required infectious dose still remains unknown. Oral infection is a common feature for both, animals and humans. However, subsequent mechanisms to access the brain are likely to differ between host species. In humans, it is assumed that *L. monocytogenes* passes the gastrointestinal barrier and spreads haematogenously to the brain (Nikitas et al., 2011; Disson and Lecuit, 2012). In ruminants, there are indications that the pathogen enters the cranial nerves via the oral epithelium or conjunctivae (Charlton and Garcia, 1977). Moving within the axons, it reaches the brain stem and spreads further to other regions of the brain via axonal pathways (Oevermann et al., 2010a; Madarame et al., 2011). Affected animals have been rarely found to show signs of systemic infections during *post mortem* examination, corroborating this local ascending route of infection (Spycher, 2012).

Gaining knowledge on the pathway of CNS infection as well as involved molecular mechanisms and risk factors, is highly important with regard to reliable disease detection as well as improvement of therapy options and prophylaxis strategies. Understanding the spread of *L. monocytogenes* into the CNS may allow the identification of specific markers and the development of molecular tools for disease detection *in vivo*. Currently, confirmation of neurolisteriosis in ruminants cannot be attained *in vivo*. Pleocytosis in the cerebrospinal fluid (CSF) as well as a positive response to antibiotic treatment provide only unspecific support to a preliminary clinical diagnosis. As opposed to humans, neither isolation nor PCR detection of *L. monocytogenes* in animal CSF has been successful and hence do not provide a reliable diagnosis tool (Peters et al., 1995). Definitive diagnosis of neurolisteriosis still requires *post mortem* detection of characteristic histological lesions and/or isolation of *L. monocytogenes* from brain tissue. Following the assumption that a large proportion of diseased animals is not submitted to *post mortem* examination, the current surveillance system in Switzerland, which is based on the notification of laboratory confirmed diagnosis, categorically underestimates the prevalence of neurolisteriosis in ruminants.

Clinical signs of CNS infection

In ruminants, incubation time for listeric rhombencephalitis is longer than for other manifestations and varies between 1 and 7 weeks. Clinical presentation depends on the localisation and distribution of lesions in the nervous system. Most commonly, the brainstem and the cranial nerves are uni- or bilaterally affected, which results in frequently unilateral palsies of cranial nerves V, VII, VIII, IX, X, XII as well as affection of the vestibular system (Tab. 1). Thus, typical clinical presentation includes difficulties in swallowing, a drooping ear or eyelid, head tilt or circling (Fig. 2). Moreover, unspecific symptoms like fever, dullness and inappetence may occur. Recumbency, convulsions and opisthotonus can be observed during fulminant disease progression frequently occurring in small ruminants, which often die within 1 to 3 days after symptom onset. In cattle, disease progression is slower with a longer overall duration of

Table 1: Affected cranial nerve nuclei and correlating clinical symptoms of *L. monocytogenes* infection in ruminants.

Affected cranial nerve nuclei	Clinical Symptoms
Nervus (N.) trigeminus (V)	– Chewing difficulties – Reduced palpebral and menace reflex – Dropped jaw – Reduced sensitivity of the head to touch
N. facialis (VII)	– Drooping eyelid, ear and lip – Reduced palpebral and menace reflex
N. vestibulocochlearis (VIII)	– Nystagmus
N. glossopharyngeus (IX)	– Swallowing difficulties
N. vagus (X)	– Swallowing difficulties
N. hypoglossus (XII)	– Tongue paralysis
Vestibular System	– Circling, head tilt, leaning towards one side

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Figure 2: Sheep affected by neurolisteriosis presenting with head tilt, chewing and swallowing difficulties, drooping ear, eyelid and lip. (Courtesy of: Clinic for Ruminants, Vetsuisse-Faculty, University of Bern)

infection and lower mortality, which could be due to a more effective immune response (Jungi et al., 1997; Oevermann et al., 2010a).

Therapy

Current therapy options of listeriosis include antibiosis and unspecific supportive care, but the mortality rate among diseased animals and humans remains high despite treatment (Braun et al., 2002; Schweizer et al., 2006; Swaminathan and Gerner-Smidt, 2007). Furthermore, treatment success remains difficult to assess as a reliable diagnosis of listeriosis can only be attained *post mortem*. In general, isolates of *L. monocytogenes* are susceptible to a wide variety of antimicrobials (Swaminathan and Gerner-Smidt, 2007). Antimicrobial resistance in clinical strains is relatively rare but has been reported for tetracycline and doxycycline (Vela et al., 2001). Interestingly, resistances appear to be more frequent in isolates from farm environments (Srinivasan et al., 2005). However, the number of systematic studies on antimicrobial resistance of clinical *L. monocytogenes* isolates, especially from ruminants, is limited.

The environment as a reservoir

The environment provides an ecological niche for *Listeria* spp. *L. monocytogenes* is commonly associated with the soil and lives as a saprophyte on decaying vegetation. Due to the wide distribution of *L. monocytogenes* and its ability to sustain and grow in plant-soil environments (Weis and Seeliger, 1975), contamination of fresh produce during cultivation and post-harvest processing poses a threat to animal and human health. Because of its high stress tolerance, growth of *L. monocytogenes* on vegetables may further increase during storage, even at refrigeration temperatures (Tian et al., 2012). Particularly high concentrations of *L. monocytogenes* in nature have been found within deer feeding areas and agricultural production systems, like croplands and livestock farms (Tham et al., 1999; Lyautey et al., 2007).

The prevalence and ecology of different *L. monocytogenes* strains in the agricultural and ruminant environment, however, are insufficiently known. Moreover, the impact of farming practices on the prevalence of *L. monocytogenes* has not yet been elucidated. Generally, it has been found that bovine farm environments yield a particularly high prevalence of *L. monocytogenes*, including subtypes linked to human listeriosis cases and outbreaks (Nightingale et al., 2004). In contrast to small ruminants, cattle appear to contribute to the amplification and spread of *L. monocytogenes* in the farm environment, which suggests that the epidemiology and transmission of *L. monocytogenes* could differ between ruminant species (Nightingale et al., 2004; Oliver et al., 2005). *L. monocytogenes* in cattle farms has a seasonality pattern with higher environmental isolation rates in spring possibly as a consequence of a combination of winter livestock housing, silage feeding and spring application of manure (Wilkes et al., 2011). This could lead to the emergence of a cycle, in which the cattle farm environment remains a constant reservoir for *L. monocytogenes*. However, this cycle and its significance for public health have not yet been fully understood. Furthermore, it needs to be elucidated whether geographic differences and different husbandry types and agricultural systems may play a role in the spread of *L. monocytogenes* between individual animals, flocks and species.

Up to now, it is unknown whether the ecology of different *L. monocytogenes* strains is distinct and the existence of ecotypes remains to be demonstrated (Vivant et al., 2013). Moreover, it is not clear whether all or only specific *L. monocytogenes* subtypes are able to get from the farm environment to the ruminant and to the consumer (e.g. by contaminating raw milk) causing disease. Consequently, there is a strong need to systematically study the prevalence of *L. monocytogenes* strains in the ruminant farm environment, raw materials (e.g. raw milk), transport vehicles and containers, manufacturing facilities (e.g. cheese factories) and personnel compared to their prevalence in infection. This will allow to identify strains that are particularly prone to reach the consumer and elucidate their transmission pathways and vectors, respectively.

Challenges in the food industry

It is estimated that up to 99% of human listeriosis cases arise from ingestion of contaminated food (Farber and Peterkin, 1991; Mead et al., 1999). As *Listeria* are ubiquitously present in the environment, initial contamination of food may occur at any stage before consumption, including primary agricultural production, food processing, retail level and consumer's homes (Wagner and McLauchlin, 2008). This eventuates in different contamination routes: either directly from raw ready-to-eat products (i.e. raw milk, cheese, fruit, vegetables), or indirectly via environmental or post-processing contamination (i.e. milk and cheese products, meat, fruit and vegetables). Consequently, *Listeria* spp. can also act as a hygiene indicator for various stages of the food processing chain.

Infections have been associated with different food production types, ranging from raw produce to complex foods like sandwiches, as well as various food types, including dairy products, meat, fish and vegetables. Affected food types commonly share the following features: they support the multiplication of *L. monocytogenes*, are processed with extended shelf life at refrigeration temperatures and do not require cooking before consumption ("ready-to-eat foods") (McLauchlin, 1996). Making their control particularly challenging, *Listeria* survive and multiply under numerous conditions that are applied in food production, preservation and storage. They are relatively resistant to acid and high salt concentrations as well as cooling, iron depletion and low oxygen conditions (Soni et al., 2011). This implies that even if only present at an initially low level, *L. monocytogenes* may further multiply in different food types during storage. Consequently, particular attention also needs to be paid during primary production (i.e. milk production) to assure specific control of the pathogen by implementing efficient milking hygiene measures and control of *L. monocytogenes* mastitis.

In Switzerland, cheese production, in particular from raw milk, is an important food industry sector. More precisely, almost half of the commercially produced milk is used to manufacture cheese, a large proportion of which is exported to other countries (Federal Office for Agriculture FOAG, 2012). This underlines the public health and economic impact that an outbreak associated with this food type might have. In the past decades, Switzerland was hit by such outbreaks twice: from 1983 to 1987 in connection with "Vacherin Mont d'Or" soft cheese, which led to a high mortality and a high number of encephalitis cases, as well as in 2005 related to "Tomme" soft cheese (Büla et al., 1995; Bille et al., 2006). As a consequence to the 1983 to 1987 outbreak the Swiss government decreed the creation of the Listeria Monitoring Program (LMP), which is still in effect today. This programme requires that milk and milk products are tested for *L. monocytogenes* as part of quality assurance programmes in cooperation with the Swiss dairy industry. The aims of the LMP are to detect contamination in cheese factories and ripening centres as early as possible, to stop the spread of *Listeria* and to prevent contaminated cheeses to be placed on the market.

According to current Swiss food legislation, *L. monocytogenes,* regardless of its strain, is required to be absent in 25g of food that promotes its multiplication or must not exceed 100 cfu/g in food that doesn't promote multiplication (Hygieneverordnung des EDI (HyV), 2005). This means that in the present system, all *L. monocytogenes* isolated from the food production chain are treated as an equally serious public health threat, even though it is known that there are many distinct strains of the bacterium, which may differ regarding virulence and infectious potential (Ragon et al., 2008). Furthermore, the infectious dose required to cause clinical disease has not been defined and whether it varies between strains is presently not known.

In the future, it will be crucial to determine virulence factors that may function as molecular markers in order to discriminate strains that are more likely to cause disease and are associated with high fatality from avirulent/less virulent strains. This will allow targeted screening for virulent *L. monocytogenes* strains in food production and, thus, improve the prevention of foodborne listeriosis. Considering the economic impact of the current policy (e.g. associated with food recalls), it would be desirable to distinctly identify pathogenic *L. monocytogenes* and specifically eliminate them from the food chain.

Moreover, databases of standardised and, thus, comparable profiles of isolates of different origin (clinical isolates of human origin, isolates out of food and feed, isolates from veterinary surveillance, isolates from the farm and factory environment) generated by use of high-resolution subtyping methods are needed. This would significantly contribute to understanding transmission pathways and help to determine possible sources of contamination in future outbreak events.

Surveillance of listeriosis in ruminants

In order to assess the overall impact of *L. monocytogenes* on the veterinary and public health system, it is important to reliably estimate the prevalence of listeriosis in the animal population. However, a large proportion of deceased animals is currently not submitted to *post mortem* examination, making it seem likely that a high number of listeriosis cases remain undetected. This could significantly influence the number of notifications of animal listeriosis in Switzerland. The current surveillance system for listeriosis relies on the report of laboratory confirmed cases only. The success of such a system is largely dependent on the farmer's level of disease awareness and the decision to contact a veterinarian as well as the willingness to comply with the recommendation for a post-mortem examination. Key factors in the decision-making process may be the cost of veterinary intervention and testing, within-herd prevalence of symptoms, value of diseased animals and concern about possible inconvenient consequences of a positive test outcome. Neurological disease in particular has been shown to be less likely reported than other symptom complexes in livestock (Gilbert et al., 2013).

During the past few years, the number of animal listeriosis cases in Switzerland was consistently low. In 2011, 15 confirmed cases of animal listeriosis (8 in cattle, 3 in sheep and 4 in goats) were reported to the authorities. In the course of clinical investigations, a total of 82 tests for *L. monocytogenes* was carried out, mostly concerning abortions and general disease (Federal Veterinary Office FVO, 2011). This low number of reported cases is in strong contrast to results from surveillance studies. In Switzerland, an extensive active surveillance study revealed that listeriosis is by far the most common CNS disease in the national adult small ruminant population and that its prevalence is highly underestimated. Furthermore, listeriosis proved to be significantly more common in animals than in humans with an estimate of 200 cases/million animals (Oevermann et al., 2008). Moreover, it is the most common differential diagnosis for BSE in adult cattle presenting with neurological symptoms in many European countries (McGill and Wells, 1993; Agerholm et al., 2002; Miyashita et al., 2004; Iulini et al., 2012). It is therefore doubtful that the number of currently reported cases displays the real prevalence of animal listeriosis in Switzerland, a fortiori because the active surveillance study did not include animals less than 1 year of age. With regard to sensitivity, it is required to re-evaluate the effectiveness of the current passive surveillance system. One possibility for improvement is the introduction of an active surveillance programme, for example by testing a representative number of fallen stock animals for listeriosis. Another option is to shift the obligation to report cases from a laboratory to a clinical level by making it compulsory for veterinarians or even livestock owners to report suspect clinical cases. Finally, introduction of syndromic surveillance, i.e. mandatory reporting of all neurologically diseased animals, would bear the advantage of also capturing differential diagnoses of listeriosis and avoid a seeming decline in the proportion of diagnosed listeriosis cases in the field if reporting on a clinical level became mandatory. Obtaining a more precise assessment of the actual prevalence of listeriosis as well as in-depth investigation of the environmental distribution and ecology of different strains would mark an important step towards finding a possible link between environmental reservoirs of *L. monocytogenes*, ruminant cases and human infection.

Conclusion

In the future, it will be essential to carry out systematic characterisation studies of *L. monocytogenes* subtypes in all 4 niches – livestock, humans, food and environment – in order to improve understanding of the pathogen's ecology. This may allow to identify possible links and transmission pathways between these niches (Fig. 1) and, in further consequence, help to prevent the infection of ruminants and humans. Discrimination between pathogenic, in particular neurotropic, and non-pathogenic strains will make it possible to take more specific control measures in the context of disease prevention and to limit economic losses associated with food recalls. Revision of the current surveillance system with regard to its potential for improvement could generate a more reliable assessment of the prevalence of listeriosis in the animal population.

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Infections à *Listeria monocytogenes* chez les ruminants: existe-t-il un lien avec la contamination de l'environnement et des denrées alimentaires et avec la santé humaine?

Listeria (L.) monocytogenes est un germe largement répandu dans l'environnement, qui peut toutefois, en cas d'infection, causer une maladie grave chez l'homme et les ruminants. Le présent article donne une vision générale de la listériose chez les ruminants et discute des actuelles lacunes de connaissances en ce qui concerne les réservoirs de *L. monocytogenes* et la possible transmission de ce germe entre les animaux, l'homme, les aliments et l'environnement. Le rôle de sous-types génétiques de *L. monocytogenes* dans l'écologie et la virulence de ce germe n'est pour l'instant que peu éclairci et les connaissances actuelles des facteurs de risque, du diagnostic *in vivo* et de la pathogénèse d'une infection à *L. monocytogeses* chez les ruminants sont insuffisantes. Il est important, pour améliorer le contrôle de *L. monocytogenes* en vue de la prévention de la maladie, de combler ces lacunes. Les présentes propositions d'améliorations en matière de surveillance de la maladie ont pour but d'optimiser l'estimation de la prévalence de la listériose chez les ruminants, cette prévalence étant actuellement très vraisemblablement sous-estimée.

Infezione nei ruminanti da *Listeria monocytogenes*: sussiste un collegamento di contaminazione dell'ambiente, degli alimenti e della salute umana?

La *Listeria (L.) monocytogenes* è un germe molto diffuso nell'ambiente che, in caso di infezione, può causare gravi malattie invasive negli esseri umani e nei ruminanti. Questo articolo vuole fornire una panoramica sulla listeriosi nei ruminanti e mettere in evidenza certe lacune delle conoscenze attuali sul serbatoio naturale della *L. monocytogenes* e della sua possibile trasmissione tra animali, esseri umani, cibo e ambiente. Il ruolo dei sottotipi genetici nell'ecologia e la virulenza della *L. monocytogenes* finora non è stato ancora chiarito e le attuali conoscenze dei fattori di rischio della diagnosi *in vivo* e della patogenesi della *L. monocytogenes* nei ruminanti sono insufficienti. Per migliorare il controllo della *L. monocytogenes* in termini di prevenzione, sarà importante in futuro colmare le lacune conoscitive. I suggerimenti di cui sopra per il miglioramento della sorveglianza delle malattie, devono avere come obiettivo di ottimizzare la stima della prevalenza della listeriosi nei ruminanti, poiché attualmente essa viene probabilmente molto sottovalutata.

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