Contagious Agalactia
Summary

Introduction

1. This note provides a brief summary of the Disease and Product analysis prepared by a DISCONTOOLS group of experts on Contagious Agalactia (CA). They reviewed the current knowledge on the disease, considered the existing disease control tools, identified current gaps in the availability and quality of the control tools and finally determined the research necessary to develop new or improved tools. Full details are available on the web site at http://www.discontools.eu/.

Disease profile

2. CA is a highly infectious disease of sheep and goats. The main pathogen is *Mycoplasma agalactiae* although recently *M. capricolum* subsp. *capricolum* and *M. mycoides* subsp. *capri* have also been implicated along with *M. putrefaciens* which causes mastitis and arthritis in goats. CA presents itself differently in sheep and goats. In sheep the disease is a less severe and is caused almost always by *M. agalactiae*, while in the goats it is a serious illness that can be caused by *M. agalactiae* and other Mycoplasmas. Clinical disease can be manifested in an acute, sub-acute or chronic form.

3. Mastitis, arthritis, keratoconjunctivitis and blindness can occur in both male and female sheep and goats. The major pathogen (*M. agalactiae*) was considered to be unusually homogenous but more recent work with variable number tandem repeat analysis of the genome has revealed unexpected diversity which it is believed is sufficient to distinguish the geographical location of any particular outbreak. Horizontal transmission occurs by contact between infected animals and/or the environment shared with infected animals. Vertical transmission can occur by means of suckling milk from infected mothers. Animals become infected by ingestion or occasionally by inhalation. Aerosol transmission is possible over short distances. Transmission via fomites (milking equipment or milker's hands) is possible.

Risk

4. Sheep and goats are the species involved. It has been shown that other animal species, such as camels, cattle, or small wild ruminants (deer, ibexes) can function as infection reservoirs. Antibodies have also been detected in South American camelids (Llamas, Alpacas, Vicunas). The precise reservoir role of common European wild animals (mammalians, birds, …) in enzootic areas is unknown. Disease is spread invariably by animal movements.

5. The disease occurs in southern Europe, Western Asia, the USA and North Africa. The current geographical location of the disease suggests it is prevalent in sub-tropical regions and climate change may enhance spread to currently clear areas.

6. The current use of antibiotics to treat the disease may lead to increased resistance among human pathogens and is an indirect risk. There is no evidence that the mycoplasmas causing CA are zoonotic though there are unconfirmed reports of sickness in humans working with calves fed goat milk naturally affected with *M. m. capri.*

Diagnostics

7. Commercial ELISA kits for serological monitoring are available, but further validation through international laboratory comparisons and development of reference sera are still recommended. Particular challenges with current ELISAs include difficulties in detecting host response early in infection and in asymptomatic animals. Should marker vaccines become available then diagnostic kits based on serology that can distinguish between vaccinated and infected animals would be useful. Serology for other causative agents of CA (goats) still relies on the complement fixation test (CFT) with expertise required to perform and interpret. There is no CFT for *M. putrefaciens*. Pen-side tests for testing milk/sera have been described but need further evaluation and need to become more cost-efficient for screening purposes.

8. A multiplex real-time PCR kit is commercially available that targets all CA agents.

Commercial diagnostic agar medium plates can assist with identification of *M. agalactiae* from mixed cultures, but this is not available for other CA syndromic organisms.

Vaccines

9. A variety of vaccines aimed at preventing CA due to *M. agalactiae* are produced and used widely in the Mediterranean countries of Europe and in western Asia. The majority are inactivated whole cell vaccines. Live vaccines are not permitted in Europe but inactivated, adjuvanted vaccines are available commercially, with inactivated autogenous vaccines also used. However, due to decreasing antibody titre as determined by available antibody detection tests, vaccination needs to be repeated at 4-6 monthly intervals (depending on product), which is expensive and often impractical. Outside of Europe, live attenuated vaccines may be used. Comparative experimental studies indicate that live attenuated vaccines, such as that used in Turkey, have greater efficacy than inactivated vaccines in experimental challenge trials. Note: Some countries free of CA will use a slaughter policy to control disease incursions, so vaccination is not permitted.

10. For goats, dual, or multiplex vaccines against *M. agalactiae* and *M. mycoides* subsp. *capri* with some also including *M. capricolum* subsp. *capricolum* are available and developed commercially. A multivalent formalin inactivated vaccine incorporating all four causative mycoplasmas was trialled experimentally and despite showing some promise (in preventing new clinical signs), was not developed commercially.

Pharmaceuticals

11. Antibiotics are used to control the disease (mainly tetracycline, macrolide, florfenicol, tiamulin and fluoroquinolones). Although the mycoplasmastatic antibiotics are effective in reducing the severity of clinical signs they may not eliminate the organism. In the short term, therapy is likely to remain with the use of antibiotics, with or without vaccination, in combination. More effective, targeted, anti-mycoplasma therapeutics are required. However, the initiatives to drive down antimicrobial use in the EU is combined with lack of new antibiotics under development.

Assessment of activity of plant-based, and other naturally occurring, antimicrobial alternatives is in its infancy, with few studies yet to include *M. agalactiae.*

Knowledge

12. The incubation period may last from one week to two or more months, with duration being related to the degree of virulence of the infectious agent and the overall resistance by the host immune system.The factors associated with reactivation of mycoplasma are not well known and need investigation. The incubation period may also be affected by immune status and stress of the host. Little is known of the pathogenicity mechanisms in particular the role of lymphatic and intracellular dissemination. The contribution of the host immune response to lesion development in mammary gland and lung and disease requires investigation.

13. Precise role of domestic and wild small ruminants (e.g. ungulates) as reservoirs is required for the development of risk-based surveillance approaches.

14. The role of pneumonia as part of the infectious / transmission process for *M. agalactiae* has not been clearly defined. Furthermore, the presence of *M. agalactiae* in the brain requires further investigated and may be responsible for ataxia seen in newly born lambs and kids. Further work is needed on the transmission mechanisms. There is a needed to confirm whether insects often present in the ears are capable of infecting rather than just carrying the mycoplasmas. Transmission of infectious fluids from the eye may occur by contact and/or by flies. In addition the significance of aerosol transmission and pneumonia preceding bacteraemia and development of mastitis should be investigated.

15. Mycoplasma lipoproteins appear to be key to inducing an adaptive host response and immune evasion enabling dissemination within the infected host. In *M. agalactiae* the surface exposed vpma lipoproteins, have a pivotal role in the subsequent adhesion, invasion and dissemination from the mammary gland, but the exact role remains to be identified.

Conclusions

16. CA can cause serious economic losses and certainly has a serious affect on animal welfare. Prevention may be by biosecurity measures and vaccination and control is by the use of antibiotics although these normally leave treated animals as carriers. Greater awareness of this little known but economically important disease should be encouraged.