DISCONTOOLS

Brucellosis
Summary

Introduction

This note provides a summary of an analysis undertaken by a DISCONTOOLS group of experts on brucellosis. 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. Details can be downloaded from the website at http://www.discontools.eu/. The gap analysis scoring on the website refers to cattle only. In addition, the expert group has provided separate gap analyses for small ruminants, *B. ovis*, swine, dogs, other domestic animals and terrestrial and marine wildlife, which can be downloaded here.

Disease profile

1. The brucellae bacteria comprise several species and infect a wide range of animals. Cattle, yaks, water buffaloes, sheep, goats, reindeer, camelids, swine, horses, hares, seals (pinnipeds), dolphins and porpoises (and other toothed whales), and dogs are known to be susceptible. Whereas *B. melitensis*, *B. abortus*, *B. canis* and *B. ovis* have well defined characteristics, *B. suis* shows a great internal diversity in terms of phylogeny/biovars and pathogenicity. In livestock and humans, the geographical range of the disease is well known but in wildlife there is much less information. New *Brucella* strains that do not fit within the classical species have been described recently from papions, frogs, bats, and from human cases, and the known range is getting wider as the organism is looked for in more host species. Unfortunately, some molecular taxonomists have included bacteria of the genus *Ochrobactrum* (free living, occasionally opportunistic in humans) in the genus *Brucella*, and such merging is reflected in data bases creating a great deal of confusion.
2. The greatest concern is the infection of domestic ruminants and swine. In this livestock, brucellosis is highly transmissible particularly in immunologically naïve flocks and herds. Infected ruminants and swine may shed brucellae via urine, but the aborted foetus, foetal membranes and fluids, genital discharges and milk are the most important sources of infection. Semen is also a source of infection. Upon contact or ingestion of infected materials, the brucellae enter the host through the mucosae and colonize a variety of organs, showing a characteristic genital tropism.
3. Brucellosis lacks pathognomonic symptoms and signs in both humans and animals. In livestock, abortion, birth of weak offspring, infertility and genital lesions in males are the most common manifestations of brucellosis. The rate of abortions varies between 0 to 40% in cattle, sheep, goats and swine, depending upon whether the disease was recently introduced in a flock/herd or the flock/herd is chronically infected. The severity of brucellosis varies according to the host and the infective species and strain.

Risk

4. Less than 20 countries (including Northern European countries, the UK, Spain and France) are free of brucellosis in domestic livestock. The movement of infected animals is the main mechanism for the spread of disease between herds. The animal disease is endemic in many areas, and this makes eradication very difficult if surrounding areas still have infections. In non-protected animals, the disease spreads very quickly. A major risk is reintroduction of the disease in areas where it has been eradicated and vaccination has been discontinued.
5. The lack of outward clinical signs of disease in animals other than abortion and fertility reduction means that detection is difficult without a sustained and expensive surveillance programme.
6. Human infection comes from contact with livestock and animal products. The populations at greatest risk are those that regularly come into contact with infected animals and those that consume unpasteurised dairy products. Although there are no reliable data on the number of human cases for most countries, a recent estimate is 2.1. millions of new cases per year.

Diagnostics

7. Bacterial culture is the only unequivocal diagnostic method to confirm infection. However, since it is slow, cumbersome, comparatively expensive, hazardous and has suboptimal sensitivity, it is only

suitable for diagnosis at herd/flock level. For animal samples, several selective media exist but none is perfect. Moreover, selective antibiotic supplement needed in some is not commercially available. Conventional typing of isolated brucellae is difficult and poses reproducibility problems and has been replaced by multiplex PCR and some other DNA analyses including those based on whole genome sequencing.

8. Several PCR protocols have been optimized for analytical sensitivity and specificity under laboratory conditions, but none has been properly validated in animal samples. In human brucellosis diagnosis, a few PCR and RT-PCR protocols has been studied but are not extensively used. These methods have not been standardized and are expensive although cheaper alternatives are in development.
9. Several immunological methods such as the Complement Fixation test, iELISA, cELISA, a fluorescence polarisation assay, Rose Bengal test, lateral flow immunochromatography and brucellin skin tests are available for the detection of infections by *B. abortus*, *B. melitensis* or *B. suis*. Many commercial diagnostic kits are available but, although costs of tests are generally competitive, distribution costs and logistics can add significant barriers to usage for many areas in Latin America, Africa or Asia. Almost all kits require cold storage, and this may be a problem in some resource poorer regions. All serological tests need validation according to local conditions and the specific animal host.
10. Information is lacking on the performance of serological tests in camelids, yaks, water buffaloes and wildlife.

Vaccines

11. The currently available vaccines are live attenuated strains. There have been attempts to produce subcellular or DNA based vaccines, but none are as practical and/or effective as the current vaccines. Vaccines are available against cattle brucellosis by *B. abortus* (S19 and RB51) or by *B. melitensis* (S19) and small ruminant brucellosis by *B. melitensis* (Rev 1).
12. There is no *B. ovis*-specific vaccine (Rev 1, the only vaccine currently available for sheep is effective against *B. ovis* but cannot be used in *B. melitensis*-free areas) or a vaccine against pig brucellosis.
13. No existing vaccine is completely safe when applied to pregnant animals, especially Rev 1 in small ruminants, and all interfere to some degree in serological tests. New safer vaccines would represent a clear advantage over the existing ones provided they confer at least the same degree or immunity as the existing ones.
14. No vaccine exists (or has been tested for protection and safety) in other domestic ruminants and camelids.

Pharmaceuticals

15. Therapy is seldom used in animals. For human brucellosis, more efficacious and cheaper antibiotics would be valued that avoid parental administration, have a shorter administration period, totally avoid relapses and make treatment more affordable.

Knowledge

16. A better understanding of the virulence mechanism and pathogenicity of brucellae and the interaction with immunity is necessary.
17. A better understanding of brucellosis in camelids, yaks, water buffaloes and other less common livestock species is needed.
18. Knowledge is lacking concerning aspects of the epidemiology and diagnosis of brucellosis in wildlife.
19. Socio-economic studies under different situations are required to prioritize interventions in developing countries.

Conclusions

20. Although tools to control the disease are available and are effective if properly and rigorously applied, safer, more effective and cheaper tools are needed. Current costs of eradication are unsustainable for most economies where brucellosis is prevalent. This implies research encompassing points 8, 10, and 12 to 19.
21. The epidemiology, diagnosis and immunoprophylaxis of brucellosis in less common livestock species needs further investigation.