Liver Fluke
Summary

Introduction

1. This note provides a brief summary of the Disease and Product analysis prepared by a DISCONTOOLS group of experts on Liver Fluke. 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/ and can be downloaded by selecting Disease Database, then the specific disease and highlighting the variables of interest. This is completed by selecting "create a report" which can then be downloaded as either a PDF or Excel spread sheet.

Disease profile

2. Liver fluke is caused by mainly *Fasciola hepatica* (*F. hepatica*) in temperate areas and *F. gigantica* in the tropics. The disease is found on every continent but is particularly prevalent in areas of high rainfall and temperatures above 10^{o}C where the intermediate snail host is abundant. The life cycle is seasonal, occurring in the winter in Mediterranean countries when conditions are suitable for development and in the summer in northern climes where the winter is too cold. Both temperature and rainfall and other environmental and physical factors have a profound effect on the incidence.

3. The severity of the disease in herbivores depends to some extent on host susceptibility but principally on the severity of challenge and number of flukes which establish in the liver. It is not clear if different isolates of fluke have differing degrees of pathogenicity but some evidence exists that some isolates are more virulent in snails and yields of cercariae are variable between different isolates thereby impacting the level of challenge animal's face. Disease incidence also varies according to the availability of the intermediate host the freshwater snail from the Family Lymnaeidae. The disease occurs in three forms – acute, sub-acute and chronic. Acute disease may lead to sudden death which is common in sheep, but does not occur in cattle, and is less common in Europe. During sub-acute and chronic disease, clinical signs usually occur as a result of the migration of immature fluke and their feeding on liver tissue causing damage to the parenchyma, anaemia and fibrosis. The adult flukes in the bile ducts feed on blood causing anaemia, cholangitis and weight loss.

Risk

4. In humans a range of trematode infections have been identified that are considered to be components of the WHO classification of Neglected Tropical Diseases. Human fascioliasis is very rare in Europe but in some parts of the world the disease is a major public health issue. The incidence of human infection with *F. hepatica* is estimated at 2.4 million with180 million people at risk.

5. Direct transmission between animals is not possible since the life cycle is dependent on maturation in the intermediate snail host. Infected animals shed eggs which develop and infect snails which results in production of cercariae which encyst on pasture. These are the infective stage for domestic and wild life hosts. Snails can be transported accidentally via a variety of routes (e.g. on wild birds) but the movement of infected domestic stock is most likely to be responsible for introduction of infection into new areas.

6. Currently the most urgent risk is the development of resistance to current pharmaceutical products. The predicted effects of climate change may also significantly increase the risk of the disease and there is the potential for an increase in the incidence of the disease among herbivores which could lead to increased risk to the human population in some areas.

Diagnostics

7. A range of diagnostic tools are available to detect infection but few are used to detect disease. There are commercial antibody detection tests for cattle but not for sheep but these detect evidence of exposure not necessarily current infection. Little information is available about how quickly antibody levels decline in response to treatment or loss of infection. Bulk tank tests are available for dairy cattle to enable herd-level estimates of exposure. There is a need for

i) pen-side tests, ii) herd level tests to identify heavily infected beef herds, iii) tests for diagnosis especially for acute infection in sheep or pre-patent infections in any host and iv) for the rapid diagnosis of recent infections before seroconversion.

8. Also commercially available are copro-antigen detection ELISAs that can be used in sheep and cattle. The modified version requires further evaluation and this test does not appear to work in horses. Faecal egg counts remain the gold standard to confirm live infection but fail to diagnose infection in the high risk pre-patent period thereby delaying appropriate management responses. Faecal egg count kits are available but whilst faecal egg counts are a useful indicator of infection these need validation for composite samples in cattle. Rumen flukes (paramphistomes) are becoming an increasing problem in some countries but diagnostics to differentiate between rumen fluke and liver fluke are not available.

Vaccines

9. There are no vaccines currently available but a number are under development. Research is required into how efficacious vaccines should be in order to have an effect in the field either on reducing transmission or generating sufficient immunity to protect the individual against disease. Integration of infection transmission reduction and disease incidence into a single protective score would be valuable in assessing the threshold for commercial viability. DIVA based vaccines are also important to reduce unnecessary treatment hence diagnostic tests to discriminate between vaccinated animals and naturally infected animals are required.

Pharmaceuticals

10. The prophylactic use of anthelmintics is currently the main method for prevention and control. There are a number of anthelmintics available, triclabendazole being the anthelmintic of choice because of its proven efficacy against young immature stages of Fasciola spp. Other than triclabendazole (TCBZ) there are no fully effective drugs against young juvenile stages of the parasite which are highly pathogenic.

11. Resistance in parasite populations to TCBZ has been reported in many countries (Australia, Europe and S. America) however a concerted effort to track the emergence and prevalence of resistance to TCBZ is needed. Integrated research into strategic treatment regimes, and subsequent re-infection diagnosis, reducing reliance on anthelmintics is required. The mode of action of current flukicides is not well understood and more work is required to investigate their modes of action and the mechanisms of drug resistance.

Knowledge

12. More information is required about the survival of environmental stages including the egg, metacercariae and infected snails, given different environmental conditions. In particular more information is required about how the predicted effects of climate and environmental change are likely to influence the survival of these different stages.

13. Little is known about immune responses to *F. hepatica* in naturally infected cattle and sheep and as a result there is a need to understand the immune responses to fluke (innate and adaptive; protective and suppressive) in naturally exposed animals. Field studies of naturally exposed animals to evaluate their immune responses, likelihood of reinfection and development of protection over time are required. Greater knowledge of the immune response to natural infection and that involved in protection, where evidence exists that it occurs, are required. Full details of the gaps are shown in the Disease and Product Analysis for Liver Fluke on the DISCONTOOLS web site.

Conclusions

14. The use of anthelmintics as a prophylactic treatment is common among conventional farms in fluke endemic areas. Good control programmes no longer reliant on the exclusive use of anthelmintic prophylaxis should be developed because of problems with drug resistance. The impact of fluke on its host's immune system needs further work especially the effect of increasing susceptibility to other pathogens leading to altered disease course and diagnosis of some infections such as bovine TB. This should be a priority area for more research.

15. There is a lack of sensitive and specific, fully evaluated diagnostics for sheep, cattle and humans. There also is a lack of drugs that are effective against the young immature stages of the parasite and there is also a lack of vaccines targeting all stages and suitable for any host species.

16. Genome mapping should be a priority area of research to: aid in identification of drug resistant isolates, mechanisms and improving our understanding of drug resistance to different flukicides; develop tools for diagnosis; and differentiating between species and identifying hybrid species.,