DISCONTOOLS

Shigatoxigenic *Escherichia coli* (STEC)
Summary

Introduction

1. This note provides a brief summary of an analysis undertaken by a DISCONTOOLS group of experts on STEC. They reviewed the current knowledge on the pathogen, 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 can be downloaded from the web site at http://www.discontools.eu/

Disease profile

2. Most *Escherichia coli* bacteria are harmless commensals; however certain strains produce potent toxins and are known as Shiga toxin-producing *E. coli* (STEC). STEC are zoonotic pathogens, occurring worldwide. STEC can cause severe human illnesses and ruminants, particularly cattle act as their natural reservoir. To date, more than 100 different serotypes have been identified as STEC, with O157:H7 and O26:H11 serotypes most commonly associated with severe human disease. Although, other serotypes, namely O104 have been prominent in the last decade.
3. STEC can cause a wide spectrum of disease in humans, ranging from mild uncomplicated diarrhoea to severe bloody diarrhoea and the haemolytic uraemic syndrome (HUS), a potentially life-threatening condition which is mainly observed in young children.
4. STEC colonisation in animals is generally asymptomatic with the exception of isolates implicated in diseases in pigs and poultry (these are not zoonotic). STEC are common in other cattle and other ruminants and have been isolated from pigs, horses, dogs, chicken, pigeon and wild birds. STEC colonise the distal gastrointestinal tract of animals and large numbers of organisms can be excreted in their faeces. STEC can persist in individual animals for several months.
5. STEC can survive in the environment for extended periods of time, reports suggest that survival can be more than 90 days in soil and months to years in manure and the farm environment. STEC can spread within the farm by direct contact, contamination of water, feed, vehicles and environment, and by other animals such as dogs, cats and wildlife. Flies appear to also play a significant role.
6. Human STEC infections can occur through exposure to extremely low infectious doses. Routes of transmission include ingestion of contaminated foods of animal origin, especially ground beef and dairy products, water and vegetables contaminated with farm slurry, direct contact with live animals, contaminated animal products or a contaminated environment. Person-to-person transmission does occur.

Risk

7. Surveillance systems are in place in industrialised areas such as Europe, North America, Japan, and Australia. In the US, the incidence is estimated to be around 100,000 cases per year. However, the prevalence and epidemiology of STEC infection is poorly known in developing countries.
8. Food sources identified as providing a risk of infection include undercooked ground beef, unpasteurised milk and dairy products and contaminated fresh produce. Good food hygiene is essential to prevent zoonotic transmission.
9. Most control efforts have been aimed at ensuring that food and water are not contaminated with STEC from cattle faeces. Prevention of colonisation in livestock is difficult. Many reservoir hosts, many routes of transmission, and the persistence of environmental contamination represent the primary obstacles for control.
10. In colonised animals, shedding of STEC is usually intermittent. However, a few animals, defined as “Super shedders” can excrete very large numbers of organisms in the faeces, and can remain colonised for longer periods. These “Super shedders” might play a major role in

maintaining and spreading the STEC within herds. These animals are also a high risk for human infection.

Diagnostics

11. In general, the laboratory tools for STEC O157 detection are adequate, while those for STEC non-O157 detection are still relatively poor. A number of PCR based assays to detect the other pathogenic serogroups (such as O26, O103, O111, O145) have been developed. More recently LAMP assays combined with lateral flow technology promise the potential for pen-side testing. Moreover, Whole Genome Sequencing (WGS) has been implemented in many diagnostics laboratories. However, these are relatively expensive, therefore rapid tests targeting the main non-O157 and O157 pathogenic serogroups are still urgently required. Moreover, rapid, economical sequence-based typing systems are also required to aid epidemiological investigations.

Vaccines

12. Experimental vaccines to prevent the colonisation of cattle with STEC O157 have been developed, but their efficacy remains controversial. A vaccine has obtained licensing approval from the Canadian Food Inspection Agency and in Europe. Another product has recently obtained a conditional approval by the U.S. Department of Agriculture. The efficacy of the available vaccines against STEC O157 has still to be fully evaluated. As infected cattle are asymptomatic there could be little demand from farmers for a vaccine. More research on non-O157 vaccines is urgently required.

Pharmaceuticals

13. In cattle, neomycin administration is effective at eliminating most O157 in cattle, but its use is complicated by the possibility of promoting antibiotic resistant organisms. In humans, antimicrobial therapy is controversial and may be contraindicated due to a possible increase in the release of Shiga toxins in the gut.
14. More research is required into therapeutics that can be used to reduce clinical symptoms in human patients.

Knowledge

15. In many countries, particularly in the developing world, the prevalence of disease due to STEC is not well understood.
16. Better knowledge of the general pathobiology and ecology of STEC is required. More information is required on the survival of STEC in soil and farm environments and the role of wildlife in the epidemiology of colonisation/infection. More research is needed on the relative importance of the different routes of transmission and sources of infection. There are gaps in knowledge on how the organism is spread between farms and how animals are exposed within a single farm. Further research is needed on animal husbandry procedures which could mitigate the risk of contamination of the environment.
17. A better understanding of the mechanisms of the pathogenesis of infection in humans and of colonisation is required. The role of past exposure and acquired immunity in relation to disease manifestation are unknown.
18. More research is required on the dynamics of colonisation in animals, including investigating the factors involved in Super shedding and determining whether tools and markers can be developed to identify Super shedders.
19. More research is required into vaccines, specifically those providing long lasting protection. More detailed studies on practical vaccine administration techniques are also required.
20. The potential of using bacteriophages, phytochemicals, novel therapeutics, prebiotics, probiotics, synbiotics and postbiotics etc. as possible approaches to control STEC should be explored.
21. More research is also required on the influence of STEC colonisation/infection on the gut microflora.

Conclusions

22. STEC can cause serious disease in humans, but the widespread occurrence of asymptomatic colonisation in animals and the widespread presence of the organism in the environment make control in livestock difficult. A better understanding of the fundamental mechanisms of the pathogenesis of infection in humans and of colonisation in livestock is required to identify the most suitable targets for diagnostics and vaccines and other novel interventions.
23. Diagnostic tests need to be improved and the availability of hundreds of STEC genomes will facilitate this. The scientific community must capitalise on the well of data already available to develop rapid, economical point of care tests.