DISCONTOOLS

Bluetongue
Summary

Introduction

1. This note provides a brief summary of an analysis undertaken by a DISCONTOOLS group of experts on Bluetongue (BT). 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 of the analysis can be downloaded from the web site at http://www.discontools.eu/ 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. Bluetongue viruses (BTVs) are present in a broad band of countries extending approximately between 40°N and 35°S although in some regions it may extend to 55°N. With the notable exception of the recently identified, horizontally transmitted small ruminant adapted BTVs, classical BTVs have been shown to be limited to regions where vector species of *Culicoides* are present and within these regions vector transmission is limited to those periods of the year when adult *Culicoides* are active.
3. BTV infects many domesticated, zoo and wild ruminants. The vast majority of infections are clinically unapparent. Clinical disease is most often seen in sheep, occasionally in goats and cattle. Severe disease can also occur in some wild ruminants. The severity of clinical signs depends on breed and immune status of the host, and is greater in naive animals/ populations.

Risk

4. The whole of Europe must be considered at risk from further incursions of BTV and other *Culicoides* transmitted orbiviruses. Local climate change could lead to increasing local temperatures, exacerbating these risks. BTV has recently expanded its geographic range and is able to cross borders due to the wide distributions of vector species of *Culicoides.* Reassortment is a frequent process that plays an important and on-going role in evolution of BTV. The continuous evolution of the BTV situation in the southern part of the Mediterranean basin poses to Southern European countries a permanent threat of new BTV strain incursions to which no immunological tools are available.
5. Classical BTVs are very stable surviving as long as 60 days in the circulation after infection of cattle, and infection persists life-long in vector insects. The virus apparently survives freezing winters. However, the mechanism behind this survival or 'over-wintering' remains unknown although vertical transmission in the mammalian host has been demonstrated and may contribute, but this is disputed. It has been proposed that BTV "overwinters" in temperate areas through low level circulation of the virus in animals and vectors, including infected adult insects that survive for relatively long periods even in winter. Conversely, atypical BTVs can survive in the circulation much longer than 60 days and for some of them horizontal transmission has been demonstrated.

Diagnostics

6. Several techniques can be used to detect the presence of BTV-specific humoral antibodies in animals which have either been infected with BTV or vaccinated against the virus. Many different antibody detection ELISA kits are commercially available including competitive and double antigen ELISAs. As these methods enable the detection of serogroup-specific antibodies in the serum and milk of infected or vaccinated animals, a 'type-specific ELISA' to detect antibodies to each BTV serotype is auspicabile. Real-time RT-PCR detection assays (group and type specific) are also available commercially from many companies. They provide a versatile system able to give information on virus serogroup and serotype within a few hours. Neither serological DIVA nor pen side tests are currently available.

7. BTV genome is *per se* highly plastic in nature, further development of existing real-time RT-PCR detection assays may therefore be required to maintain effectiveness to detect new BTV isolates/variants. In this context, the latest techniques of genome sequencing (NGS) and data analyses have been and are fundamental. NGS is becoming the most prevalent sequencing technique. Harmonization of procedures devoted to amplify the full-length of each genome segments of BTV isolates or straight from biological sample by NGS is required.
8. More effective diagnostic protocols by multiplexing existing or novel diagnostic assay systems are also requested to better detect mixed infection. Initial studies indicate that chip based technologies to detect viral RNA, can be used to identify members of the BTV group and each serotype. These technologies will need further development, but commercialisation will depend on cost and ease of use.

Vaccines

9. Although a number of vaccine strategies have been investigated with promising results, nowadays, live attenuated and inactivated vaccines remain the only vaccines commercially produced and used to prevent BT. If produced and used properly, they can successfully control and, in some circumstances, eradicate the infection. All of the current monovalent live or inactivated vaccines are however type specific. Cross-protection can only be generated by serial vaccination with multiple serotype vaccines. More effective and cross-serotype subunit-vaccines that are DIVA assay compatible and generate a stronger immune response from a single inoculation are essential. These would be particularly welcome in areas where multiple types are circulating and causing disease. They could also be used in a wider eradication campaign.
10. The “next generation” strategies, many with DIVA capability, did not have the chance to be launched on the market or tested on a large scale. No incentives exist for producers to develop and produce in anticipation of crisis. Vaccine producers need incentives to develop, test and produce vaccine for a non-existent market.

Pharmaceuticals

11. No specific treatment is available, other than supportive care. However, the potential for use of antiviral agents to induce immediate protection post infection should be explored even if there might be some problems in both developing and licensing such products and uncertainty whether they will play a major role in protection against BTV infection in the field.

Knowledge

12. One of the main features of BTV is its ability to change characteristic and behaviour and to adapt to new environments and episystems. Dealing with it implies, most of the time, to expect the unexpected and to continuously adapt our understanding. For this reason, even though BTV has been studied for many years, there are still many significant areas of uncertainty in the understanding and knowledge about the disease especially in relation to pathogenesis, immunology, vaccinology, epidemiology and control. Research is needed to fill these gaps in relation to immunity, strains and isolates, transmission and spread, reservoirs, carriers and geographical distribution in order to have a better understanding of the BTV which is closely linked to the more detailed research requirements to develop effective tools for the control of the disease. Full details of the gaps are shown in the Disease and Product Analysis for Bluetongue on the DISCONTOOLS web site.

Conclusions

13. Bluetongue disease (BT) represents an important threat to livestock health and food production in Europe and neighbouring countries. Surveillance as well as vaccination remain the principle tools for prevention and control, depending on the context. The continuing arrival of new ‘exotic’ strains from neighbouring regions, however, suggests that incursions by BTV (and possibly by related orbiviruses and other arboviruses) are likely to continue in Europe for the foreseeable future.

14. New serotypes and new potential vectors have been identified, an additional non-structural viral protein has been revealed, as well as the capability of some field strains/serotypes to be transmitted either vertically or horizontally, to alter their pathogenicity, host specificity, and capacity for spread. Reassortments between field strains, vaccine strains, and between field and vaccine strains have generated and will continue to generate novel genotypes. The potential for these progeny strains to be transmitted more effectively and to have increased virulence poses significant additional risks for ruminant health. Thus, the continued evolution of BTV strains poses a substantial challenge to the research community. Within this context, it is then crucial to engage in a continuous dialogue among researchers, laboratories, and policy-makers in order to gain a deeper understanding of new developments, increase mutual knowledge, and share a unique and integrated strategic approach.