A spotlight on Bluetongue virus?

In the late 1990s, there were rumblings that Bluetongue virus (BTV) was on the move. The 2006 summer outbreak changed the way that the European economic and scientific communities viewed its importance. It shifted from being a neglected disease confined to the tropical regions of the world to a potentially important threat to agriculture. Suddenly, BTV was sharing research priorities and the limelight with other important viruses of animals such as foot-and-mouth disease virus and avian influenza virus.

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Just as BTV had changed its geographical location in 2006, I had also moved across oceans and continents from Australia to the United Kingdom to study this virus. In the last 10 years I have been lucky enough to be involved with the increased understanding and technological advancements that have ensued due to the impact of a highly pathogenic virus entering a new environment.

The importance of BTV

BTV is a member of the Reoviridae, a family that includes the diarrhoea-causing rotavirus. But, unlike rotavirus, which is transmitted via the faecal-oral route, BTV transmission occurs between
therefore, without these biting midges BTV would not be able to spread from animal to animal. But there is a newly identified strain (BTV-26) that may be transmitted via direct contact.

The clinical symptoms of Bluetongue disease depend on viral strain, host species and even animal breed. In general, sheep are the most susceptible to disease, in particular, breeds of European descent. Typically, the disease presents as an acute period of high fever (5–7 days), excessive salivation and sweating, laboured breathing, swelling of the face and, in ~10% of cases, a cyanotic (blue) tongue. Not all sheep develop clinical signs, but those that do rapidly lose condition, with the sickest generally

ruminant animal hosts (e.g. sheep, cattle) via biting midges (Culicoides species) taking a blood meal. For those readers that live in Scotland or in Western Australia, you may be all too familiar with these swarming, biting insects that use you as their own personal summer smorgasbord. Classically, BTV is non-contagious;
dying within a week. Associated with the disease are severe increases to production costs, as the recovery of affected animals is slow, while high fever in sheep results in poor quality wool.

The European outbreak (2006–2008) is noteworthy as BTV displayed new characteristics. First, this novel strain, BTV-8, was exceptionally virulent, with fatalities in sheep reaching 40%. Furthermore, BTV-8 could also induce clinical signs in cattle. The virus also crossed the placenta and caused disease in the foetus; something that had only been observed with certain live BTV vaccine strains. From an epidemiological perspective, BTV-8 was being transmitted exclusively by European midge species that had not previously been shown to be capable of sustaining an outbreak.

The impact of the BTV-8 outbreak was devastating. In addition to direct losses, regions where BTV is endemic or where outbreaks occur are now subject to international trade restrictions; the economic cost of the 2007 BTV outbreak in France was $1.4 billion and $85 million in the Netherlands.

**Changing locations**

Historically, BTV had been confined to regions between 40˚ N and 35˚ S latitudes, including Africa, the Middle East, India, China, the United States and Mexico. Although BTV is also endemic in South-east Asia, Papua New Guinea, northern South America and northern Australia, these countries are considered to be free of clinical disease by the World Organization for Animal Health. This is in part due to the particular sheep breeds present, or a lack of sheep present in the endemic regions of these countries. In Europe, Bluetongue disease was considered exotic with sporadic cases localised to the Mediterranean Basin until the late 1990s. Although outbreaks can sometimes be attributed to animal movement, encroachment into naïve territories is primarily due to the windborne dispersal of BTV-infected midges. This allows expansion of the virus over large geographical areas (e.g. from Indonesia to Australia). In Australia BTV spread has been predicted to be due to the climatic conditions (e.g. wet, warm springs), while in Europe the size of the midge population/susceptible animal populations are critical factors. Recently, an Oxford group showed that 38% infection of BTV during 2006 was due to midges moving upwind under their own power. These findings have implications for other viruses and pathogens spread by biting midges.

The increased incidence of BTV in new environments is a clear indication that the geographical location of BTV is expanding. The source of the outbreak of BTV-8 in northern Europe is still unknown. It may have been introduced by different mechanisms other than the wind-assisted movement of infected Culicoides species. This includes the movement of infected livestock, use of live attenuated vaccine strains and the importation of midges with flowers or fresh produce. Furthermore, unlike the previous movements of the virus throughout Europe, BTV-8 expanded from Northern Europe (i.e. Belgium, France) into Italy and Spain, crossing the major physical barriers of the Swiss Alps and Pyrenees mountain range.

Traditionally, spread of BTV in Europe was linked to the geographical distribution of the African midge (Culicoides imicola), which has extended northwards as a consequence of climate change. The ability of the midge to be infected by BTV (vector competence) was always postulated to be a factor that hampered BTV’s geographical spread. Infection of European midges (Culicoides obsoletus and C. pulicaris) was often associated with a lag time where other BTV strains had to ‘adapt’. BTV-8 infection of the European Culicoides species did not display this lag time. These viral characteristics may have assisted the rapid spread throughout Europe.

**Geographical change of BTV research**

The emergence of BTV into northern Europe placed a spotlight on the BTV research community to rapidly respond and provide a solution. The biggest factors identified with enabling BTV to spread throughout Europe were strategies to identify and control the spreading outbreak, and the lack of suitable vaccines. The use of live attenuated vaccines in Italy had proven to be troublesome. Just as the virus had dispersed, scientists like myself were travelling through Europe as part of a collaborative research network.
Importantly, diagnostic tests with rapid turnaround times were developed. This led to the identification of new types of BTV and a system to identify all circulating strains of BTV. The advancement in vaccine development was aided by molecular tools to manipulate the virus, and protein expression tools. The research group I belonged to was involved in developing and testing new vaccines with DIVA (discriminate between vaccinated and infected animals) potential to limit the impact of trade restrictions.

This network of scientists provided a greater understanding of virus–host interactions and factors that enabled BTV outbreaks to occur (weather, midge population, etc.). Importantly, these results aided in the rapid response to another midge-transmitted virus of sheep (Schmallenberg virus) in Europe years later. Although a wealth of knowledge has been generated, there are still big questions to be tackled, with the threat of a new outbreak always present.

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Further reading