Several species of anaerobic spirochaetes belonging to the genus *Brachyspira* (formerly *Serpulina*) are of considerable veterinary significance, causing diarrhoea and poor growth rates in various animal species – most notably in pigs. The best-known species is the strongly *β*-haemolytic *Brachyspira hyodysenteriae*, causing a severe mucoshaemorrhagic colitis known as swine dysentery. In recent years, as diagnostic techniques have been improved, the potential role of some of the other weakly haemolytic *Brachyspira* species in animals has been recognized. In humans, the role of *Brachyspira pilosicoli* and *Brachyspira aalborgi* as colorectal pathogens has started to receive more attention. This special issue contains a selection of papers presented at the 2nd International Conference on Colonic Spirochaetes, held near Edinburgh in April 2003. By publishing these articles here, our aim is to give a flavour of current research and thinking about these bacteria and their potential to cause disease in animals and man. Currently, the state of research on *Brachyspira* lags well behind that of many other bacterial genera. The ability to manipulate the spirochaetes genetically is limited, and there are relatively few research groups working on these micro-organisms. Most researchers are based in veterinary institutes, and nearly all are still attempting to identify and delineate the various species and to study their distribution and disease associations. Much of the published work is therefore concerned with the epidemiology, diagnosis and control of the various *Brachyspira* species, rather than attempting to understand pathogenic mechanisms or spirochaete biology. This editorial briefly summarizes some of the findings from these papers and attempts to put them in perspective. Areas requiring more work are highlighted.

Appropriately, given its economic impact, the issue starts with papers relating to *B. hyodysenteriae*. Swine dysentery remains an important endemic disease in many pig-rearing countries, where control is limited by a lack of effective vaccines and by the emergence of spirochaete strains with reduced susceptibility to antimicrobials. One impediment to vaccine development is the relatively poor understanding of the basis of immunity to swine dysentery. In the first paper, Jonasson and colleagues describe a study investigating levels of circulating leukocytes and lymphocyte subpopulations in pigs before and after experimentally induced swine dysentery. By comparing results from pigs that did or did not succumb to disease, the authors deduced that γδ T cells and CD8⁺ cells may be associated with susceptibility to infection, whilst monocytes and CD4⁺ CD8⁻ T cells appear to be the major responding lymphocytes. These results add to previous information about CD8⁺ cell proliferation in pigs recovered from swine dysentery (Waters et al., 2000) and provide background information that could help to evaluate immunological responses to new vaccines being developed for swine dysentery. Jacobson and colleagues then describe efforts to reproduce swine dysentery in pigs reliably, and identify factors involved in disease susceptibility. Group-housing and feeding large quantities of soybean meal resulted in development of swine dysentery in pigs in a study conducted in Sweden (Jonasson et al., 2001). In a second paper, Jonasson and colleagues use a similar approach, but with an extended duration of soybean meal feeding, to determine the pathogenic potential of these spirochaete described by Jansson and colleagues. It will also be important to confirm the species identity of the spirochaete described by Jansson and colleagues. Further work, particularly using DNA–DNA reassociation assays, is required in order to confirm the species identity of the spirochaetes described by Jansson and colleagues. It will also be important to determine the pathogenic potential of these avian *B. hyodysenteriae* isolates in experimentally infected pigs. The main practical significance of the work is the possibility that these strains could act as a source of infection or reinfection for pigs, especially since wild mallards may travel large distances during their migration.

The papers by Karlsson and colleagues and Lobova and colleagues emphasize the increasing problem in Central/Eastern Europe of strains of *B. hyodysenteriae* with decreased susceptibility to veterinary pleuromutilin drugs (tiamulin and valnemulin). Until recently, these drugs have been effective and widely used for controlling swine dysentery. This reduced susceptibility, which Karlsson and colleagues show is not simply the result of the spread of a single spirochaete clone, is of considerable concern. The decreased susceptibility is suspected to have arisen from prolonged and/or subtherapeutic use of tiamulin in piggeries. To reduce the spread of resistant strains, it will be important to limit the between-herd movement of colonized strains and to tighten controls on the use of these and other important antimicrobials.

In recent years, widespread problems associated with weakly haemolytic intestinal spirochaete species that cause ‘avian intestinal spirochaetosis’ (AIS) in commercial adult laying and breeding chickens have been documented (Stephens & Hampson, 1999). Although the problems of AIS are not covered by papers in the issue, the manuscript by Jansson and colleagues describes the presence of *B. hyodysenteriae* and other strongly *β*-haemolytic and indole-positive spirochaetes in mallards. This is an important and somewhat contentious paper, since it represents the first description of *B. hyodysenteriae* in birds (other than in farmed rehas). The paper emphasizes the somewhat blurred boundaries between some of the current *Brachyspira* species, especially the indole-positive spirochaetes (*B. hyodysenteriae* and *B. aalborgi*). The species delineations were originally formulated largely in the context of porcine spirochaetes, and these definitions may not always hold when the diverse groups of intestinal spirochaetes that colonize birds also are considered. Further work, particularly using DNA–DNA reassociation assays, is required in order to confirm the species identity of the spirochaetes described by Jansson and colleagues. It will also be important to determine the pathogenic potential of these avian *B. hyodysenteriae* isolates in experimentally infected pigs. The main practical significance of the work is the possibility that these strains could act as a source of infection or reinfection for pigs, especially since wild mallards may travel large distances during their migration.

The paper by Corona-Barrera and colleagues addresses the problem of detecting the two main porcine pathogenic spirochaetes (*B. hyodysenteriae* and *B. intermedia*).
Dietary influences on colonization. This paper unifies several on standard diets were not susceptible to containing lactose and zinc bacitracin. Mice were tested for spirochaete colonization. The paper by Jensen and colleagues describes extensive colonization of pigs with B. pilosicoli following experimental infection. This spirochaete is widespread in pigs and is associated with mild colitis and reduced growth. Unlike most other Brachyspira species, B. pilosicoli can be used as one of the best examples of how dietary influences can affect colonization in pigs. The study indicates that B. pilosicoli can have considerable pathogenic potential under certain circumstances. No attempt was made to look for B. pilosicoli in humans, which has been identified in immunocompromised humans in a number of studies (e.g. Kanavaki et al., 2002).

The paper by Jamshidian and colleagues describes a model in which human isolates of B. pilosicoli colonized mice fed on a diet containing lactose and zinc bacitracin. Mice on standard diets were not susceptible to colonization. This paper unifies several ideas about the need for predisposing factors in intestinal spirochaetal infections. Dietary influences on B. hyodysenteriae and B. pilosicoli infections in pigs have been described previously, and B. pilosicoli colonization in chickens is enhanced by zinc bacitracin. By analogy, it seems possible that dietary influences on colonization could help to explain the uneven distribution and sporadic occurrence of human intestinal spirochaete-associated disease. Mouse models should prove useful for studying pathogenesis and immune mechanisms in B. pilosicoli infections (Sacco et al., 1997).

Few data are available about virulence mechanisms possessed by intestinal spirochaetes. The haemolytic activity of B. hyodysenteriae is considered important for pathogenicity in swine dysentery, whilst end-on attachment of B. pilosicoli or B. aalborgi may be associated with microvillus damage and a physical obstruction of absorption. In their paper, Dassanayake and colleagues describe a model in which B. pilosicoli and speculate that these may represent virulence determinants. Further work is required to determine whether disruption of this proteolytic activity reduces virulence.

Continuing the theme of human infection with B. pilosicoli, Margawani and colleagues describe an epidemiological study of B. pilosicoli in humans on the island of Bali, Indonesia. Overall prevalence of faecal carriage was relatively high (~12%), and varied from 3 to 23% depending on sampling location. Colonization was most common amongst individuals in a crowded peri-urban area. Colonization was associated with the use of well water, and affected individuals had an increased chance of having wet faeces. This study confirms that colonization with B. pilosicoli is common in humans in developing communities (Trott et al., 1998) and there is evidence of the spirochaete having a considerable burden on human health in many regions.

The paper by Mikosza and colleagues analyses genetic variation in B. aalborgi, the second species that colonizes humans. As this spirochaete is difficult to isolate, partial 16S rDNA and NADH oxidase gene sequences were amplified from fixed colorectal epithelium to allow an analysis to be undertaken. Sequence analysis confirmed the existence of two clusters of B. aalborgi-like spirochaetes in humans, with cluster 1 isolates being typical B. aalborgi and cluster 2 isolates perhaps representing a novel, uncultivated species. Cluster 3, identified previously by Pettersson et al. (2000), was not detected, but a new cluster (cluster 4) restricted to isolates from non-human primates was identified, and almost certainly represents a novel Brachyspira species. Clearly, these sequence-based techniques are proving important in identifying new groups of intestinal spirochaetes that otherwise are difficult to isolate and identify by conventional methods. Use of these methods may ultimately link specific Brachyspira species to specific human diseases. On the same theme, Jensen and colleagues describe the use of in situ hybridization to detect evidence of ‘lineages’ (or, to be consistent, ‘clusters’) 2 and 3 in human colonic biopsies. This elegant technique will be particularly useful for studying the distribution of these spirochaetes in the human large intestine and their specific association with pathological changes.

The final paper describes the use of 16S rDNA sequence analysis together with biochemical testing to identify intestinal spirochaetes from dogs. Besides confirming that dogs may be colonized by B. pilosicoli and ‘Brachyspira canis’, three isolates clustered with the type strain of Brachyspira alvinipulli. The latter spirochaete is an (uncommon) pathogen of chickens, and hence this finding is both new and of considerable interest. Further work is required to confirm this species identity and to determine whether the canine isolates of B. alvinipulli have pathogenic potential in chickens.

These papers give an indication of the general interest and focus of current work on intestinal spirochaetes. At the conference, a plea was made to mobilize resources to start whole genomic sequencing studies on representatives of the main species. Currently, a lack of genetic information about these spirochaetes represents a bottleneck that is hindering progress. In addition, for effective control of intestinal spirochaete infections, it was evident that further work is required to understand the colonization processes with the various Brachyspira species and how these may be influenced by dietary, immunological and other factors.


