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One Health: parasites and beyond…

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Introduction

The field of parasitism is broad, encompassing relationships between organisms where one benefits at the expense of another. Traditionally the discipline focuses on eukaryotes, with the study of bacteria and viruses complementary but distinct. Nonetheless, parasites vary in size and complexity from single celled protozoa, to enormous plants like those in the genus *Rafflesia*. Lifecycles range from obligate intracellular to extensive exoparasitism. Examples of parasites include high profile medical and zoonotic pathogens such as *Plasmodium*, veterinary pathogens of wild and captive animals and many of the agents which cause neglected tropical diseases, stretching to parasites which infect plants and other parasites (e.g. (Blake *et al.*, 2015; Hemingway, 2015; Hotez *et al.*, 2014; Kikuchi *et al.*, 2011; Meekums *et al.*, 2015; Sandlund *et al.*, 2015). The breadth of parasitology has been matched by the variety of ways in which parasites are studied, drawing upon biological, chemical, molecular, epidemiological and other expertise. Despite such breadth bridging between disciplines has commonly been problematic, regardless of extensive encouragement from government agencies, peer audiences and funding bodies promoting multi-disciplinary research. Now, progress in understanding and collaboration can benefit from establishment of the One Health concept (Stark *et al.*, 2015; Zinsstag *et al.*, 2012). One Health draws upon biological, environmental, medical, veterinary and social science disciplines in order to improve human, animal and environmental health, although it remains tantalizingly difficult to engage many relevant parties. For infectious diseases traditional divides have been exacerbated as the importance of wildlife reservoirs, climate change, food production systems and socio-economic diversity have been recognised but often not addressed in a multi-disciplinary manner.

In response the 2015 Autumn Symposium organized by the British Society for Parasitology (BSP; https://www.bsp.uk.net/home/) was focused on One Health, running under the title 'One Health: parasites and beyond…'. The meeting, held at the Royal Veterinary College (RVC) in Camden, London from September 14th to 15th, drew upon a blend of specialist parasitology reinforced with additional complementary expertise. Scientists, advocates, policy makers and industry representatives were invited to present at the meeting, promoting and developing One Health understanding with relevance to parasitology. The decision to widen the scope of the meeting to non-parasitological, but informative topics, is reflected in the diversity of the articles included in this special issue. A key feature of the meeting was encouragement of early career scientists, with more than 35% of the delegates registered as students and 25 posters.

One Health?

There is no formal definition of One Health but at its core is the promotion of animal, human and environmental health through cross-disciplinary working. Taking a historical perspective, this concept is far from new. Until formal veterinary training was established in the 18th century, human health practitioners often treated animals (Currier & Steele, 2011). In the 19th century, the German physician and statesman Rudolf Virchow coined the term "zoonosis" and stated that "between animal and human medicine there are no dividing lines - nor should there be" (Kahn *et al.*, 2007). However, in the 20th century there was an ever increasing separation between human and veterinary medicine. It was only in the second half of this century that the close relationship between humans, animals and public health was again recognised through the work of the Canadian epidemiologist Calvin Schwabe (Schwabe, 1984), where he formalised the concept of "One Medicine" – a general medicine of human and animals.

The emergence of a number of zoonotic viruses with pandemic potential in the early 2000s led to a recognition of the need for greater collaboration across disciplines including human and veterinary medicine, wildlife biology, environmental science, anthropology, economics and sociology to prevent infectious disease emergence and spread (Gibbs, 2014). At a meeting of the Wildlife Conservation Society in 2004, the term "One World-One Health™" was introduced to encompass medicine and ecosystem health, and the Manhattan principles were established promoting a holistic approach to preventing disease emergence and spread, and maintaining ecosystem integrity (Calistri *et al.*, 2013). Since then, the One Health approach has gathered significant momentum, receiving official endorsement from the European Commission, the World Bank, World Health Organization (WHO), Food and Agriculture Organization of the United Nations (FAO), and the World Organization for Animal Health (OIE), among others (http://www.onehealthglobal.net).

Current definitions of "One Health" abound. The Food and Agricultural Organization describes it as "A collaborative, international, cross-sectoral, multidisciplinary mechanism to address threats and reduce risks of detrimental infectious diseases at the animal-human-ecosystem interface" (http://www.fao.org/ag/againfo/home/en/news_archive/2010_one-health.html), whereas the American Veterinary Medical Association takes a broader approach: "the collaborative efforts of multiple disciplines working locally, nationally and globally to attain optimal health for people, animals and our environment" (https://www.avma.org/KB/Resources/Reference/Pages/One-Health94.aspx). The One Health Initiative definition follows in a similar vein, describing One Health as "a worldwide strategy for expanding interdisciplinary collaborations and communications in all aspects of health care for humans, animals and the environment' (http://www.onehealthinitiative.com/about.php). In contrast Zinsstag *et al*. proposed an operational definition of One Health focusing on the added value in terms of human and animal health or cost savings or environmental and social benefits that can be achieved through professionals from different disciplines working together (Zinsstag *et al.*, 2012). It has been suggested that the flexibility of the One Health concept is part of its success as it can be adapted to suit the missions of different organisations (Gibbs, 2014).

One confusing aspect of the varying definitions of One Health is the apparently interchangeable use of the words "multidisciplinary" and "interdisciplinary". These terms actually have different definitions with "multidisciplinary" referring to projects involving experts from different disciplines who remain within their area of expertise over the course of the project. Interpretation and integration of results from different disciplines often occurs only at the end of the project. In contrast, in "interdisciplinary" projects, experts from various fields collaborate closely throughout the course of the project, integrating and synthesizing ideas and methodologies from different disciplines with the potential to generate new research questions and approaches (Conrad *et al.*, 2013; Eigenbrode *et al.*, 2007; Moore *et al.*, 2011). Going beyond interdisciplinarity, a “transdisciplinary” approach cuts across disciplines where project participants use a common conceptual framework integrating theories and methods of different disciplines to address a shared problem. Participation of community members and key stakeholders in developing the conceptual framework and shared approach is an important aspect of transdisciplinary projects (Allen-Scott *et al.*, 2015; Min *et al.*, 2013). It has been argued that the One Health approach is transdisciplinary by its very nature (Mazet *et al.*, 2009) and certainly the application of transdisciplinarity to One Health projects has great potential (Min, 2013).

The British Society for Parasitology Autumn Symposium, 2015

This special issue contains a series of invited reviews drawn from the BSP Autumn Symposium. The first, provided by Pete Kingsley and Emma Taylor, introduces the concept of ‘One Health’ and considers what the term actually means (Kingsley & Taylor, 2016). An enormous volume of activity has been advertised as One Health; some merely rebranding existing pursuits, others pushing at fundamental boundaries and genuinely creating new connections. The control of African trypanosomiasis provides an historic example of One Health in action, even before the birth of the term. The authors highlight the importance of improved information and fairer approaches, expanding the remit of assessments beyond individual specific medical, veterinary or environmental concerns. Assessing not only the impact of pathogens and interventions, but also the intrinsic value of human and animal welfare, food safety, security, and the environment, provides a natural entrée to the paper presented by Rushton and Bruce in this issue (Rushton & Bruce, 2016). The need for flexibility is emphasised, with views evolving as more information becomes available or situations change.

Building on an understanding of One Health it becomes clear that assessing losses caused by parasitic disease, even if we incorporate the direct cost of controlling the disease, fails to reveal the true impact. For human pathogens disability adjusted life years (DALYs) have been developed to provide a single measure of total disease burden, presented as the number of years lost as a consequence of ill-health, disability or early death (Fernandez Martin *et al.*, 1995). Despite creation of the DALYs measure the true cost of many diseases of humans remains underestimated, with the inaccuracy magnified for zoonotic diseases where veterinary costs are commonly poorly defined. Further, difficulty quantifying indirect costs such as resources used or lost, impact on services and other social or environmental factors adds yet more uncertainty. In their paper presented here Johnathan Rushton and Mieghan Bruce assess the approaches which might be taken to identify One Health variables and include them in a quantifiable metric (Rushton & Bruce, 2016). Taking avian coccidiosis caused by the protozoan *Eimeria* species as an example, the authors begin to explore application of quantifiable One Health cost matrices. The cost attributed to coccidiosis may be as high as $3 billion per annum, although estimates vary by tenfold or greater (Blake & Tomley, 2014). Indicators of environmental and social impact are suggested for inclusion in forthcoming quantitative analysis.

There have been increasing reports of emerging infectious diseases (EIDs) over the past few decades. EIDs include new diseases caused by novel pathogens, such as the highly-publicised emergence of severe acute respiratory syndrome (SARS) in China in 2002, and existing diseases which spread into new areas, as exemplified by the recent outbreak of Ebola virus disease in West Africa. In their review, Bryony Jones, Martha Betson and Dirk Pfeiffer contend that anthropogenic changes to the global ecosystem are drivers of disease emergence and identify important eco-social processes which may play a role including human population growth, urbanisation, increasing mobility and connectedness, inequality, increasing consumption, habitat destruction, biodiversity loss and climate change. They go on to illustrate the impact of human activity on emergence of infectious diseases using examples from different continents. Finally, given the complexity and connectedness of the eco-social processes which can drive disease emergence and spread, the authors argue that management of disease threats requires a systems-based One Health approach, citing appropriate theoretical frameworks which could be adopted.

In a more practical offering Rachel Chalmers and colleagues recommend development and agreement of a standardized genotyping approach for *Cryptosporidium* diagnosis, surveillance and outbreak investigation (Chalmers *et al.*, 2016). *Cryptosporidium parvum* is a major cause of livestock and zoonotic cryptosporidiosis. Morphological approaches are limited to genus-level identification, as indicated by the relatively recent differentiation of species such as *C. parvum* and *Cryptosporidium hominis* with molecular and epidemiological support (Abrahamsen *et al.*, 2004; Xu *et al.*, 2004). Sequence analysis of targets including the 18S ribosomal DNA and glycoprotein 60 (gp60) were widely employed and offer value for money (Cardona *et al.*, 2011; Chalmers *et al.*, 2011). Greater detail has been achieved using multi-locus sequence typing (MLST), although the relative cost is greater (Ramo *et al.*, 2014). Recent protocols which support whole genome sequencing of *Cryptosporidium* isolated directly from faecal samples may well replace these tools in time (Hadfield *et al.*, 2015), but at present cost-effective, robust and reproducible assays are urgently required to facilitate comparison of results between studies and laboratories. Currently, variable number of tandem repeat (VNTR), and associated variation in polymerase chain reaction (PCR) amplicon size, offer a reasonable solution. In the work presented Chalmers *et al*. compare a panel of nine VNTR-based markers across multiple samples assessed in three different laboratories. They found some loci to present unexpectedly complex repeat units, weakening their value to routine analysis, and take a significant step towards standardization of tools for molecular *C. parvum* genotyping. At this time it is clear that additional markers are still required as the research community drives towards a consistent nomenclature for these parasites.

Stepping back in time, Piers Mitchell's article demonstrates how a combination of parasitology, anthropology and historical research can provide insights into human infection and disease in previous generations (Mitchell, 2016). He focuses on the Roman Empire and investigates whether "Romanisation" altered the balance of parasitic infection in people living in Europe and the Mediterranean region. Interestingly, despite substantial improvements in hygiene and sanitation during this period, gastrointestinal parasites such as *Trichuris* and *Ascaris* infections were widespread and fish tapeworm and ectoparasites such as lice and fleas were also present. The author discusses these findings in relation to what is known about the Roman diet and farming and bathing practices. He also reflects on what Roman physicians believed about intestinal worms and how to treat them. This article provides an excellent illustration of how different complementary disciplines can be successfully integrated to address a research question.

The neglected tropical diseases and neglected zoonotic diseases have received increasing attention over the past few years and new goals have been set for control and elimination at a regional and global level (WHO, 2012). One such neglected zoonosis is *Taenia solium* taeniosis/cysticercosis (TSTC), which the World Health Organization (WHO) considers to be an eradicable disease and has decided to target for elimination in certain endemic countries (WHO, 2015). In their article Maria Vang Johansen and colleagues reflect on why no endemic country has managed to eliminate *T. solium* (Johansen *et al.*, 2016). They identify a number of factors including an inadequate understanding of social factors which influence transmission and the fact that neither the medical nor veterinary services want to take responsibility for control. The authors then describe a theoretical model of *T. solium* transmission in an endemic area and use this model to predict the effect of various intervention strategies on taeniosis in humans and cystercercosis in pigs. Based on model simulations, an integrated One Health approach combining interventions in humans and pigs would be able to reduce disease significantly in both species. However, this approach does not appear to be sufficient to achieve elimination of TSTC, thus highlighting the need to set realistic targets for control, before aiming for elimination.

Over the last decade the relevance of animal reservoirs to the (re)emergence of infectious agents has become well defined (Morens *et al.*, 2004). Protozoan parasites have been highlighted as posing a particular risk in contrast to helminths (Taylor *et al.*, 2001), possibly a consequence of the latter's greater complexity, longer generation time and size. Nonetheless, novel helminths have been described. Hybrid and/or introgressed *Fasciola* derived from *Fasciola hepatica* and *Fasciola gigantica* have been described across much of Asia with relevance to veterinary and human health (Le *et al.*, 2008). Similarly, hybridization and/or introgression between *Schistosoma* species has been well documented in recent years and is now reviewed here by Elsa Leger and Joanne Webster. The authors review multiple examples of hybridization between *Schistosoma* species which traditionally infect humans, livestock, and humans and livestock. Intriguingly, reports of hybrid schistosomes date back many decades with multiple examples from the 1950s and 1960s (Leger and Webster, 2016). The authors describe the ways in which hybrid schistosomes have been defined, including egg morphology and several molecular approaches, before focusing on possible drivers towards hybridization such as human interventions like dam construction and changes to farming which impact on the snail intermediate host, as well as the selection imposed by mass drug administration. The emergence of novel parasite genotypes with expanded host ranges and/or altered pathogenicity bears obvious significance to human and veterinary medicine, once again posing problems in the assessment of cost and development of effective control(s).

Zoonotic parasites are a global concern as demonstrated in Celia Holland's article (Holland, 2015). This review provides a comprehensive overview of the latest research into the biology, epidemiology and public health impact of the roundworm *Toxocara* and highlights the important gaps which exist in our understanding of this cosmopolitan parasite. The author describes the multiple manifestations of toxocariasis in humans while stressing the difficulties of diagnosing this disease and of linking exposure to clinical presentation. The important role which vets can play, both in treatment of infected animals and in education of pet owners and the general public about the importance of *Toxocara* as a zoonotic infection, is discussed. The review draws attention to our poor understanding of the relative contribution of paratenic hosts and environmental contamination with fox, dog and cat faeces to *Toxocara* transmission and illustrates how mathematical modelling approaches can shed light on this question. Finally, the author proposes a One Health framework for research into this enigmatic parasite.

In the final paper of this special issue Shazia Hosein and colleagues review the current understanding of adaptive and innate immune responses against *Leishmania* infection in dogs. The outcome of infection by many *Leishmania* species is strongly influenced by the nature of the initial immune response. Induction of a predominantly Th1-type immune response, featuring CD4+ T cell expansion and elevated interferon gamma (IFNγ) production, commonly associates with a positive outcome as the host controls the infection. Contrastingly, induction of a Th2-type immune response correlates with susceptibility to infection, with interleukin (IL)-4 a key determining factor (Hosein *et al.*, 2016). The authors provide a thorough, organ by organ summary of immune responses induced during *Leishmania* infection in dogs, before discussing the small number of anti-*Leishmania* vaccines currently available for dogs in some markets.

Conclusion

The necessity of combining medical, veterinary and environmental strands in order to improve opportunities to resolve global health concerns coalesced into the One Health concept more than ten years ago as an evolution from One Medicine (Zinsstag *et al.*, 2012). Nonetheless, despite the rapid proliferation of peer reviewed manuscripts within the One Health remit effective integration remains a challenge. In a recent systematic review social network analysis of interdisciplinarity in One Health publications revealed three distinct, albeit overlapping communities representing ecologists, veterinarians and a diverse assembly of population biologists, mathematicians, epidemiologists, and experts in human health (Manlove *et al.*, 2016). Recognition of these persistent gaps, as well as the resultant opportunities, has prompted establishment of One Health educational openings in many institutions and societies such as the British Society for Parasitology. Improved interactions between academia and other stakeholders, including medicine, animal production, health and food user groups, can fast track global development and implementation of innovative science, and promote dissemination of key outputs. Examples include assessment and development of integrated pathogen monitoring, evaluation and control strategies, as well as development of novel research proposals supported by access to new research partners.

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