Neglected zoonoses: forgotten infections among disregarded populations

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Elie Wiesel stated “the opposite of love is not hate, but indifference”, and within the following collection of reviews we focus our attention upon neglected diseases among forgotten people that are currently met by global disregard. Increasing initiatives are being launched to combat “neglected zoonoses”, but when we attempt to decipher our understanding of this term, things become less clear. We are convinced that readers of this editorial will all be able to name a selection of neglected zoonoses, but these lists are likely to differ and the inclusion criteria for selection will reflect different knowledge, perspectives and experience. When tasked with coordinating the reviews herein, I sought to define what are neglected zoonoses? The dictionary definition for neglected refers to “not receiving proper attention; disregarded” (on-line Oxford dictionary). Regarding zoonoses, the accepted dogma is generally infections derived from other vertebrates, but does not necessarily exclude those that flow in both directions (anthroponoses and zoonoses).

As this general group of infectious agents embraces the aetiological causes of up to 70% of emerging infectious diseases, and an estimated 50% of all infections, the topic is vast. Strict compartmentalisation of pathogens into such categories can be challenging as some can be transmitted by multiple

routes such as the helminth *Hymenolepis nana* that utilise humans as their definitive host and reservoir, but can also be transmitted through zoonotic routes such as utilisation of rodents as intermediate hosts, and finally also through arthropod transmission with the *Tribolium* beetles serving as the host for cysticercoids and potential foodborne human infection [1]. Indeed to assess the impact of these differing sources requires detailed understanding of sub-species genotypes of *H. nana* and host-pathogen interactions. The review by Thompson considers the possibility of different genotypes specific ecological correlations underscoring the need to fully appreciated pathogen ecology to determine risk for human infection.

For others, the human host represents an accidental host, thus the infectious agent is often not fully evolved to this unexpected environment. It is in such circumstances that we observe induction of overwhelming host immunological responses often with fatal consequences. An example of such infection is that of *Tararomyces marneffei* that causes penicilliosis and results in 100% mortality amongst immunocompromised human hosts. This neglected mycosis is the third most frequently encountered opportunistic infection among HIV-infected individuals in endemic areas such as Thailand, yet recognition of the impact of this infection is remarkably over-shadowed by other infections [2]. Though initially described associated with bamboo rats, increasing evidence suggests a role for dogs potentially providing the conduit by which humans gain exposure, with up to 40% of dogs yielding this fungus from nasal swabs in the absence of clinical consequences [2].

Further diagnostic challenges are presented by infections that lack pathological hallmarks. Determination of disease incidence is problematic particularly in those infections that are chronic or occur in locations of high endemicity such as scrub typhus [3].

Anthropogenic activities coupled with globalisation effects have facilitated rapid spread of such infections. Some that are newly emerged such as SARS-CoV and MERS-CoV and more recently Ebola virus, receive significant attention, often fuelled through fear of the unknown properties of such infections such as spread, virulence and lack of appropriate controls or interventions [4]. However, sadly many of the neglected zoonoses have plagued mankind throughout the years do not have this added novelty of being new, and are often overlooked. This neglect stems from several aspects, they are not new, and their greatest burden impacts upon those that live in close proximity to animals, which often equates to those living in poverty that are all too frequently overlooked. Here, these infections are a major cause of both morbidity and mortality, yet little research funding is channelled towards understanding the ecology, burden of disease or efficacy of control or intervention strategies.

Our traditional approach of considering individual infections may also be out-dated. Polymicrobial infections are being increasingly recognised as having significance in influencing patient outcome through exacerbation of clinical consequences. Methods used to assess the impact of different infections struggle to embrace the full complexity of single infections let alone the

complexity of polymicrobial scenarios. These inadequacies coupled with lack of proper surveillance, diagnostic limitations, and the plethora of clinical presentations following infection make assessment of the burden of disease challenging to conceptualise. This further perpetuates the lack of research funding as the impact of these infections is poorly quantified.

In consequence, limited resources allocated to such neglected zoonoses and clinical signs often overlap with other more high-profile infections such as malaria, resulting in poor discrimination of the individual infections. Intervention effectiveness might be maximised by taking a more holistic approach and extending this to control and intervention. Indeed, this is highlighted by the review by Welburn et al
[5].

Technological improvements have enabled us to differentiate emerging species or even highly successful clones within species. Indeed the emerging importance of the dog/cat hookwork *Ancylostoma ceylanicum* have only been discernable with the application of molecular diagnostics [1]. Indeed the previously unappreciated prevalence of *A. ceylanicum* might account for reduced success of hookworm mass treatment campaigns directed towards humans [1]. Looking ahead, the introduction of multi-pathogen screening and whole genomic sequencing studies is likely to reveal greater understanding of the complex and dynamic microbial-(vector)-host interactions, that will enable us to decipher the interplay between microbes and these diverse

environments, potentially providing “one health” measures for effective reduction of disease burden.

To reach this point, we need sufficient recognition of the impact of neglected zoonoses, as this is the means whereby resources will be directed towards their control. A multitude of reasons explored within the following reviews have prevented full appreciation of the significance of neglected zoonoses, but what is the solution to this dilemma? Here we could potentially follow the lead given by those involved with tackling the antimicrobial resistance issues, whereby engaging renowned economists to assess the predicted costs of inaction has facilitated constructive discussion among multiple stakeholders [6]. The few studies to quantify the economic impact of neglected zoonoses conducted to date have given alarming findings, such as the estimated global burden of 750,000 disability adjusted life years for Dengue virus alone [4]. This metric is not ideal to capture the full impact as reviewed [5], and fails to incorporate other impacts such as negative impacts upon income streams such as tourism [4]. Certainly the model of using development Impact Bonds described by Welburn appears to be successful in bringing much needed resource to tackle neglected zoonoses, but the battle is far from over [5].

References:

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