Journal of the British Global and Travel Health Association, vol 28 2017 1-2
doi: http://dx.doi.org/10.21864/jbgtha.2017.27

Commentary: Infectious diseases in Travel and Global Health - are we meeting the needs?

Prof. Larry Goodyer MPharm MRPharmS Phd FFTMRCPS(Glasg) FRGS FISTM
Chair: British Global and Travel Health Association

The recent Zika and Ebola epidemics have drawn attention to the global threat presented by infectious diseases. There is a strong relationship between global health issues where such infections can spread across international borders and in preparing the traveller overseas when entering environments where such diseases may be endemic. My own interest for the last 25 years has been in the field known as Travel Medicine and I have been involved in the pharmaceuticals, vaccines and other products that help to protect those visiting overseas; in many cases these are the same products that would be used to protect and treat the local populations living in such countries. One particular example where this is the case are those strategies that are employed to protect against biting insects. Those diseases spread particularly by the mosquito do still present a major challenge to global health e.g. malaria and dengue. Thus the same strategies used to protect the traveller overseas against biting insects could be used to protect local populations. In the case of vaccine development the two needs may not always be met in the same way; in the case of the traveller a high level of personal protection would be required but a vaccine simply conferring a level of herd immunity or giving a modest reduction in the incidence in children might be acceptable for local immunisation programmes. In this commentary, I am going to examine the requirements and gaps in the current provision of agents that are used to prevent, rather than actually treat, infectious diseases that are of direct relevance to both travel and global health by focussing on insect repellents and vaccines.

In considering first those infectious diseases spread by insects, the most important preventative strategy will be bite avoidance. Reducing the risk of being bitten by a mosquito involves a number of strategies: covering up any exposed skin with clothing which could be impregnated with insecticides and sleeping under bed nets, area methods to reduce mosquito numbers by spraying or vapourisng insecticides and applying a repellent to exposed skin. There are also various environmental methods to reduce mosquito populations by treating any surface waters that could present breeding grounds. Focussing on insect repellents, N,N-diethyl-3-methylbenzamide (DEET) has been in use since the 1950s and does remain the gold standard. In fact there are only two other widely used synthetic repellents that have a reasonable evidence base: 2-(2-hydroxyethyl)-piperidinecarboxylic acid 1-methyl ester (icaridin), and ethyl butylacetylaminopropionate (IR3535). A third effective repellent was derived from the lemon eucalyptus plant from which the active component p-methane 3, 8-diol (PMD) has been identified and produced synthetically. These are all marketed in a vast range of active ingredient (ai) strengths and formulations, including those that have an extended time actions by microencapsulations.

The efficacy is commonly, though not exclusively expressed, in terms of the time taken before mosquitoes to bite or land on an individual. That time is dependent upon many variables of environment and individual 'attractiveness'. Identifying the 'best' ai is not easy as testing procedures in the literature are very poorly standardised so it is difficult to compare the findings of one study with another. There is certainly a need to have available a greater range of effective repellents as well as novel formulations that give a longer and more consistent full protection under a range of conditions. Research has been focussed on identifying those agents produced in the human body that attract mosquitoes on which to base repellent formulations, but there have been no new repellent actives on the market since the early 2000s.

Insecticides for treating nets and clothing still rely largely on pyrethroids and there have been some reports of a reduction of efficacy in treated bed nets used to reduce malaria incidence in Africa. Resistance is not actually responsible in this case, but a change in mosquito feeding habits. The African Anopheles mosquito has been predominantly an indoor night time feeder i.e. passing the malaria parasite to individuals in particular on retiring to sleep. Due to the widespread use of bed nets the Anopheles mosquito is tending to feed earlier in the evening and out of doors, thus making the use of effective repellents an important preventative measure. Indeed mosquitoes in South America have always tended to feed more in this way and at least one study has shown a reduction in malaria incidence when repellents are used by the local population. The Aedes mosquito responsible for Zika and dengue also tends to feed in the daylight hours, highlighting a need for new repellents that are ideally affordable and acceptable to local populations.

The other major overlap between travel medicine and global health issues concerns vaccine-preventable diseases. We now have a range of vaccines for many such diseases that are used in endemic populations

Commentary *continued*

and also travellers. There are those that most countries will use in childhood vaccination schemes such as Measles/Mumps/ Rubella (MMR) and Tetanus/Diphtheria/Polio (TdP). Examples of others that may be included in vaccination programmes are hepatitis A and B, meningococcal meningitis A, C, W and Y and yellow fever. Many of these now provide long if not lifetime protection after primary immunisations. For instance conjugated hepatitis A vaccine is effective for 25 years or longer and yellow fever vaccine which is a live attenuated vaccine, was previously thought to require a booster at ten years but is now known to confer lifetime protection. Similarly, recent work has demonstrated a possible lifetime protection after primary courses of modern rabies vaccine, though post-exposure vaccination is still always essential. Meningococcal vaccines have seen recent vast improvements where now the conjugated vaccines are more widely used than the polysaccharide forms, the former being more effective in children and longer lasting. It is probably in the area of those diseases largely contracted via contaminated food and water that the most development is required. The typhoid vaccine has a low efficacy of around 70%, is not effective against paratyphoid and needs a three yearly repeat dose. Cholera vaccine, an oral formulation, also similarly has a relatively low efficacy and also needs boosters after two years in adults and just six months in those under 5 years of age. Serious epidemics of cholera and typhoid do still occur particular in regions where public health infrastructures breakdown, particularly in disaster or war situations resulting in overcrowding such as in refugee camps. Undoubtedly the greatest need is for an effective vaccine against childhood diarrhoeal illnesses that continue to claim many thousands of lives globally. Certainly, such a vaccine would be of use to travellers as diarrhoeal illness is the most likely of conditions to be experienced to many destinations. Another urgent requirement is for a more effective vaccine is against dengue fever and the related chikungunya, although a dengue vaccine offering some limited protection has been developed and undergone clinical trials it is only licensed in a few regions. There are emerging diseases such as Zika which require vaccine development and an effective Ebola virus in preparation for further outbreaks.

In terms of the treatment of infectious diseases there are major global health issues related to antimicrobial resistance. The most effective means of overcoming these problems is the use of preventative measures some of which this commentary has discussed. There are certainly areas requiring development and research which have been highlighted.

This has been adapted and reproduced with permission from an article in Chemistry World published 31st March 2017 www.chemistryworld.com