

## **CLINICAL PRACTICE**

## Public health and vaccines — immune responses in developed versus poor countries

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Immunologists and parasitologists have detected differences between individuals in developed and so-called developing countries in respect of the manner in which the immune system reacts to antigens. This should be of particular interest to health professionals in Africa, where immunisation has been described as 'the greatest public health gift we can offer children'.<sup>1</sup> Research-wise, variation in the post-vaccination immune response could well make the results of vaccine trials extremely difficult to interpret correctly. What is important from a practical point of view is that vaccine efficacy in developing countries may frequently be compromised, for reasons given below.

For instance, deficiency of zinc in the diet is widespread in underdeveloped regions, where it is responsible for a defective T-helper cell type 1 (Th1) response,<sup>2</sup> because of decreased production of interferon-gamma and interleukin-2. Perhaps better known is the theory that reduced exposure to infectious diseases in developed countries in modern times has, because of resultant changes in immune function, led to an increased prevalence of atopy compared with that in developing parts of the world, where exposure to various bacterial and viral pathogens is greater.3 Important qualitative and quantitative differences between Africans and non-Africans in relation to Tcell cytokine production have been reported.45 Furthermore, host genetic differences can be a source of variation in cytokine levels within the same population.6 This lack of uniformity could be of significance for immune intervention strategies and relevant to the design of vaccines. Whereas the response to vaccines in developing and developed countries may differ, it must be emphasised that factors such as those mentioned above have not yet actually been shown to affect vaccine efficacy. On theoretical immunological grounds, however, it

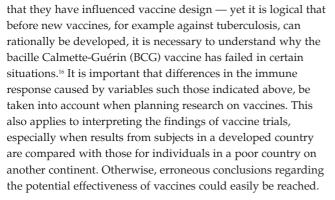
Miles Markus is Director of Biomedical Analysis International in London, UK, and has recently been contracted part-time in New York for 3 years. He was formerly Director of the Parasitology Research Programme at the University of the Witwatersrand, where he is now an Honorary Professor. Miles qualified as a medical parasitologist at Imperial College, University of London, and at the London School of Hygiene and Tropical Medicine. He is also a graduate of the universities of Pretoria and the Witwatersrand. would seem that they might do so by downregulation of the immune reaction, something that is not widely appreciated; and cognisance should be taken of this probability.

Crohn's disease, which characteristically occurs in industrialised societies, serves as another example of how the nature of the immune response can apparently depend upon whether people live in an economically developed country or in a Third-World country. The pathogenesis of this inflammatory bowel condition is currently thought to involve over-reaction of the immune system to an unknown environmental agent(s). A predisposing genetic factor may be involved. It has been suggested that a reason why Crohn's disease is rare in tropical areas with poor sanitation is that the Th2 gut mucosal response provoked by the parasitic worms which are ubiquitous in such areas leads to modulation of immune reactions to other stimuli.78 Similarly, there is evidence that enteric helminthiasis affects the gastric inflammatory response in Helicobacter pylori infection, which may partly explain the contrasting immune reactions and differing patterns of progression of this disease in the developed and developing worlds.9,10 Of course, Crohn's disease and H. pylori infection are by no means the most important public health problems in developing countries. They merely serve to illustrate how one condition might influence the immunological response to another or to a vaccine.

It is not yet common knowledge that Th2-orientated immune activation in chronic helminthiasis results in a diminished response to certain kinds of vaccines against several diseases. These include cholera, diphtheria, tetanus and tuberculosis.<sup>11</sup> The same may apply to particular types of HIV/AIDS and antimalarial vaccines.<sup>12,13</sup> The immune mechanisms that lead to protection after vaccination determine vaccine efficacy in individuals who are Th2-polarised before vaccination. These mechanisms differ and it is not always clear what they are for any given vaccine. In the case of oral vaccines, local mucosal changes caused by the presence of worms in the gut might play a role in reducing vaccine efficacy. Anthelminthic treatment before vaccination has been shown to enhance the postimmunisation response to vaccines against more than one bacterial disease.<sup>14,15</sup>

To at least some extent, these phenomena may explain why vaccines often elicit poor immune reactions in people living in developing regions, although the reasons are likely to be multifactorial. They have not yet been clarified to the extent

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Disadvantaged children in poor countries derive great benefit from immunisation against various diseases and vaccination remains 'the greatest public health gift we can offer children'.<sup>1</sup> Anthelminthic interventions also have positive health benefits in communities where the prevalence of intestinal helminthiasis is high. Consideration now needs to be given to whether immunisation against non-helminthic diseases and deworming should sometimes go hand in hand, but with the possible negative consequences of deworming on the prevalence of allergic and other conditions being taken into account.<sup>1721</sup>

Support from The Wellcome Trust, UK, is acknowledged.

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