Investigating Interactions between HIV Infection and Tropical Diseases

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Infections with the human immunodeficiency viruses (HIV) are likely to have a profound effect on the health of those in the developing countries over the next several decades, especially in Africa where the prevalence of HIV infections has become very high in some areas. The health of those in these countries is compromised already by the enormous load of illness and death due to combinations of malnutrition and the major endemic diseases. Tuberculosis is one of the most important diseases of adults in many developing countries and there is mounting evidence that HIV infections increase greatly an individual's susceptibility to this disease. Little is yet known about the interactions of HIV with other diseases in the tropics; if there are significant such interactions the overall impact of the HIV epidemic may be even worse than is predicted currently. Furthermore, it is possible that the present methods for prevention or treatment of these tropical diseases will be compromised in the presence of HIV infections.

The following are important areas for further research: Firstly, to determine what are the important interactions of HIV with the endemic tropical diseases. Secondly, to investigate whether concurrent HIV infections affect the efficacy of therapeutic or preventive measures against those diseases and, thirdly, to develop, where necessary, improved control strategies and tools. Epidemiological studies are likely to feature prominently in the identification and quantification of the interactions.

In considering the interaction of any two infections questions of the following form are of concern: To what extent does the presence of one of the infections affect the susceptibility to the other and/or influence the natural history of that infection (eg by changing the spectrum of severity, clinical manifestations, response to treatment or infectivity to others). For example, is a person infected with HIV more susceptible to malaria? After inoculation by infected mosquitoes are such people more likely to develop parasitaemia or clinical symptoms of malaria than those similarly inoculated who are not infected with HIV? Among those infected with HIV is the clinical course of malaria abnormal or different in severity? Is the malaria more or less susceptible to treatment? The small number of studies conducted to date have not provided evidence that HIV infections have an adverse effect on malaria, but further studies are needed.

Conversely, it is of interest to know whether there is an interactive effect of malaria on HIV infection. Are those with malaria more susceptible to infection with HIV? Does an attack of malaria, or even asymptomatic parasitaemia, influence the course of HIV infection? Does it precipitate clinical manifestations of HIV infection? Does it act as a trigger for the development of AIDS? How do patients with AIDS respond to malaria? Are they more or less susceptible to treatment?

These kinds of questions, and many more, can be posed in various forms with respect to the interactions between HIV infections and each of the tropical diseases. The likelihood of particular forms of interaction will vary from disease to disease and may also depend on host factors (eg age, pregnancy, malnutrition).

Figure 1 is a schematic representation of the components of the possible interactions between tropical diseases and HIV infections that are of interest. For most of the tropical diseases an individual may be in one of three states, represented by the boxes at the top of the figure. A person may be uninfected, infected but not diseased, or infected and diseased (ie having clinical symptoms of the infection). The distinction between the last two states is not always clear; for some infections there may be a continuum, with heavier infections producing clinically more severe symptoms. Individuals may pass from one state to another — from uninfected to infected to diseased and, if sufficiently severe on to death. For some infections,
such as malaria, passage between different states may go in either direction; disease manifestations may be reversed and the infection eliminated, especially with treatment, whereas for others the transitions tend to be unidirectional. For example, those infected with tuberculosis may recover from the disease but never lose that infection. The possible transitions between the infection and disease states are represented by horizontal arrows in the diagram. For some conditions, such as leprosy, we cannot presently distinguish between uninfected and infected individuals, other than through the presence of disease. For other conditions infection without disease may be very rare (e.g. T. b. rhodesiense infections).

At the foot of Figure 1 individuals are shown as being in one of three states with respect to their HIV status. In concept these states are similar to those shown for the tropical diseases, with a continuum between HIV infection without symptoms to progressive more severe forms of HIV-related disease. Horizontal arrows are shown to represent transition between the different states, with dotted arrows to represent the possibility of transition from disease to no disease and infection to no infection, though at present such transitions, if they occur at all, are very rare.

The vertical and diagonal arrows in the body of Figure 1 illustrate possible interactions between the tropical disease and HIV infections. For example, the arrow from the infected state for the tropical disease to the uninfected HIV state represents any effect that the infection with the tropical disease agent may have on the susceptibility (or exposure) to HIV infection. The arrow from the (tropical) disease state to the uninfected HIV state represents any effect on susceptibility to HIV that the clinical tropical disease might have. Also infection with the tropical disease may increase the rate of progression from HIV infection to disease. Similarly HIV infections might increase the susceptibility to infection with the tropical disease agent, might increase the probability that an infection progresses to disease or might increase the severity of the disease.

The vertical and diagonal arrows which are shown as dotted represent the possibility of interactions to or from the HIV diseased state (AIDS). At present, the health consequences of being in this state are sufficiently serious that any interactions are likely to be of minor additional public health importance, though they may be important with respect to the survival time of those with AIDS.

The evidence for significant interactions between HIV and most tropical diseases is presently scant. A reason for this may be that most of the tropical diseases have their major impact in rural areas, whereas HIV infections have been most prevalent so far in urban centres. Furthermore, the group most affected by many of the tropical diseases is young.
children and not the sexually active young adults and young infants at risk of HIV infection. As the epidemic of HIV infection spreads, however, any interactions with tropical diseases will become more important and monitoring for such effects will be essential. A variety of different studies are needed, some will be relatively simple to conduct and will give answers quickly, but others will be complex studies involving the careful follow-up of large numbers of individuals over long time periods. Initial studies should focus on interactions that seem most plausible biologically and which are likely to be of greatest public health significance. If there is an unexplained rise in the incidence or severity of a specific disease in an area where HIV infections are prevalent, a possible interaction effect should be a priority for investigation. Similarly, if the progression from HIV infection to AIDS appears to be occurring more quickly in any area, then clinical data on AIDS patients should be monitored for the occurrence of other infections which may be triggering the disease.

The United Nations Development Programme/World Bank/World Health Organization Special Programme for Research and Training in Tropical Diseases (TDR) and the WHO Global Programme on AIDS (GPA) recently sponsored a meeting at the Kenya Medical Research Institute to bring together experts on AIDS and on the major tropical diseases. The objectives of the meeting were to review what was currently known about the interrelationships between HIV infections and the tropical diseases, to draw up a list of priorities for research and to outline study designs aimed at addressing these research issues. A document is available from TDR/GPA that summarizes the proceedings of the meeting and that contains the outline protocols that were drawn up. Those interested in conducting field research studies aimed at investigating possible interactions are invited to request copies of the document from either of the Directors of the two WHO Programmes.

REFERENCES