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EDITORIAL

Toward a Unified-Field Theory of the Pathogenesis of Acquired Immune Deficiency Syndrome

As is well known, the current "mainstream" position on the relationship between infection with the human immunodeficiency virus (HIV) and the development of acquired immune deficiency syndrome (AIDS) is that the former is the sole and sufficient cause of the latter (1). Currently, there are two views that are at odds with that position. One is that the HIV is not causal of AIDS in any way and its presence in the many cases in which it does appear is entirely a matter of coincidence (2). The other contrary view is that the HIV is necessary but not sufficient for the development of AIDS. This theory holds that AIDS will develop in HIV-infected persons only if one or more cofactors compromising the effectiveness of such persons' immune systems are or have been present (3, 4).

After a lengthy period in which supporters of neither alternative theory could achieve much in the way of notice or consideration, an active, increasingly publicized debate among these three factions is now developing. Unfortunately, this debate is producing an increasing amount of heat, but not a corresponding increase in light.

Each side can present voluminous amounts of data to support its position (1–3). There are apparently otherwise completely healthy persons who, upon infection with the HIV, go on to develop AIDS and die (1). At the same time there also appear to be some otherwise healthy persons who, upon infection with the HIV, do not and most likely will never develop AIDS (5).

There are also many persons who, following infection with HIV, go on to develop AIDS and subsequently die but happen to have or have had one or more other diseases or conditions that have previously compromised their immune systems. (In this context, such diseases or conditions are known as "cofactors." They include chronic sexually transmitted disease, chronic bowel infection, chronic fungal infection, and habitual intravenous drug use.) Finally, there appears to be an increasing number of persons with a condition clinically resembling AIDS who are HIV-antibody negative and have no other evidence of HIV infection, present or past (2).

On this landscape of conflicting claims, the debate continues to rage. Each of the three sides presents its data, often accompanying such presentations with much pounding of fists upon the table. Sadly, while the debate rages on, we continue to be able to do relatively little about either the spread of this dreaded syndrome or its progression to eventual death in any individual who does develop it. But each side is convinced that its view of AIDS pathogenesis is *the* correct one, that there is nothing but bad science in each of the other two camps. The proponents of the mainstream position are absolutely convinced that theirs is the correct one, and if they are simply allowed to continue their research and clinical work at the present well-funded level, the answer will soon be found.

But supposing, just supposing, that each of the three sides is correct—each in part? Could it be that the theory to which each subscribes does in fact describe the route by which some significant proportion of the total population afflicted with AIDS came to be so afflicted, but does not describe the natural history of the developement of the syndrome in each and every case? I think that that may be so, and I would like to offer an hypothesis to that effect.

This "unified-field" hypothesis of AIDS pathogenesis holds that there is not just one pathogenetic route to that clinical condition called AIDS. Rather, as is the case, for example, in diabetes and obesity, the unified-field hypothesis of AIDS holds that there are several different pathogenetic routes leading to a similar clinical expression. One is HIV infection per se, one is HIV infection in the presence only of one or more cofactors compromising the immune system, and the third is AIDS developed entirely in the absence of detectable HIV infection.

In the present debate, each side can present a strong argument for its position but at the same time cannot completely discredit either of the other two positions. This situation would seem to lend credence to the hypothesis and in my view makes it a worthwhile candidate for investigation. If it is correct, AIDS policy would likely be affected significantly, of course.

Proving or disproving this hypothesis requires the undertaking of significant epidemiological research that has not yet been done. It would be necessary to study the distribution of HIV-antibody positivity, ongoing HIV infection, and AIDS and the person, time, and place associations of each, over time, in the general

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population, not only in special populations, as has been the case to date. The currently unanswered questions concerning the epidemiology, pathogenesis, and natural history of AIDS range from what factors if any (genetic perhaps) lead to the development of AIDS in some otherwise healthy infected persons but not in others, to what factors, perhaps environmental, are leading to the occurrence and spread of non-HIV AIDS.

Considering the possibility of the latter, one can take note of the recently observed sharp declines in the numbers of species of songbirds and frogs in many parts of the world (6, 7). Could these declines be due to as yet unknown forms of aviary and amphibian acquired immune deficiency syndromes produced, perhaps, by man-made environmental toxins of one sort or another?

What is needed now is the diversion of some money (probably not too much in the context of the sums currently being spent on AIDS research in the United States) away from virus lab work to work in field epidemiology. A major, technically quite difficult, but nevertheless necessary study is of the progression/nonprogression to AIDS over time of a sample of otherwise completely healthy persons who are HIV-antibody positive.[1] I can only hope that the debate over that rather mundane money matter will not degenerate into the same kind heat-, not light-, generating conflict that currently characterizes discussions of AIDS theory.

[1] I would like to note that I have neither a professional nor a personal self-interest in this matter: I do not do such research.

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