Symposium: Newly Emerging Viral Diseases: What Role for Nutrition?

Nutrition and Newly Emerging Viral Diseases: An Overview

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ABSTRACT Infectious diseases are on the increase worldwide. When discussing interactions of nutrition and infection, nutritionists have traditionally considered only the effects of diet on the host. Recent data, however, indicate that, at least for an RNA virus, host nutrition can influence the genetic make-up of the pathogen and thereby alter its virulence. This symposium was organized to alert the nutrition community to this discovery and its possible implications for the investigation of nutrition-infection interrelationships. Topics covered in the symposium include the following: the public health threat of emerging viral diseases; the rapid evolution of viral RNA genomes; oxidants and antioxidants in viral diseases—disease mechanisms and metabolic regulation; and increased virulence of coxsackievirus B3 due to vitamin E or selenium deficiency. If the findings with coxsackievirus are more broadly applicable to other RNA viruses, the results could be of great public health significance because RNA viruses constitute the majority of all plant, animal and human viruses. J. Nutr. 127: 948S–950S, 1997.

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Infectious diseases are back. The World Health Report 1996 of the World Health Organization declared that almost onethird of the 52 million deaths that occurred in 1995, most of them of young children, were caused by infectious diseases (Holden 1996). Deaths from infectious diseases increased by 58% between 1980 and 1992 in the United States (Pennisi 1996). According to Hiroshi Nakajima, Director-General of the WHO, "We are standing on the brink of a global crisis in infectious diseases" (Koenig 1996).

The role of host nutritional status in determining resistance to infection has long been recognized. In their extensive monograph, Scrimshaw et al. (1968) emphasized the multifactorial etiology of disease and pointed out that disease causality should be viewed as a complex triad of interacting determinants: disease agent, host characteristics and environmental factors. The emphasis in this symposium will be on nutrition as the primary environmental factor, but it should be understood that overall environmental effects need to be considered to obtain a comprehensive assessment of the influence of these extrinsic factors on disease (e.g., toxins in the diet, climate, population density, socioeconomic stability or lack thereof) (Lilienfeld 1976). The importance of good nutrition in promoting resistance to disease was underscored recently by WHO’s development of an approach to the integrated management of sick children in which the patient’s illness is addressed as a combination of problems including malnutrition, rather than only as a single disease (Anonymous 1995).

In the past, epidemiologists have regarded the effects of poor nutrition on resistance to infection as occurring solely through damaging effects of a bad diet on the host (Scrimshaw et al. 1968). That is, malnutrition was thought to interfere with various physical barriers or immune responses, thereby rendering the host more vulnerable to microbial attack. No one had stopped to consider the possibility that host diet might have some direct effect on the pathogen itself. However, the recent data of Beck and colleagues (1994a, 1994b, 1994c and 1995) show that, at least in a rodent model of enteroviral disease, this can indeed be the case. When a benign strain of coxsackievirus B3 was inoculated into mice that were deficient in either selenium or vitamin E, it was found that the virus had converted to a virulent strain that had a nucleotide composition that was different at several sites from that of the input virus. Thus, the traditional view of nutrition-infection interrelationships (Fig. 1, top) has to be replaced by a new paradigm that allows for direct effects of host nutrition on pathogen virulence (Fig. 1, bottom). The purpose of this symposium was to call the attention of the broader nutrition community to these novel insights of Beck and co-workers and to the implications of these findings in general for the study of malnutrition and infectious disease.

The symposium was led off by Stephen S. Morse of the Rockefeller University, who discussed the public health threat of emerging viral diseases (Morse 1997). Professor Morse has contributed greatly to our understanding of the concept of emerging diseases and was instrumental in setting up a global surveillance system via the Internet to monitor disease outbreaks around the world. He defined emerging diseases as those...
that either are newly appeared in the population or are rapidly increasing their incidence or expanding their geographic range. Several examples of recently emerging viral infections were presented, and these, like the coxsackievirus infection studied by Beck and colleagues, are due to RNA viruses: Ebola, Marburg, Dengue, Hantaan, Lassa, influenza and of course, HIV. This was followed by a general discussion that highlighted factors responsible for the emergence of infectious disease, such as ecological alterations wrought by economic development and land use, human demographics and behavior, international travel, technological changes and breakdown in public health measures. Professor Morse stated that host nutrition as a factor in emerging diseases has often been neglected even though microbial adaptation and change are not. Given the fact that the results of Beck et al. demonstrate the critical role of host nutritions in driving viral evolution, it is hoped that nutritional factors will gain more prominence in the future.

The second speaker on the program was Esteban Domingo of the Universidad Autonoma de Madrid who, like John Holland and Manfred Eigen, has done much to clarify our ideas about the rapid evolution of RNA virus genomes (Domingo 1997). The high mutation frequencies in RNA viruses (10⁻⁵-fold or more greater than those in their DNA-based hosts) occur because of the lack of any proofreading enzymes to correct for errors made during RNA biosynthesis. Thus, there is an enormous genomic diversity in any population of RNA viruses and any given “RNA virus” actually exists as a so-called quasispecies population (i.e., as a swarm or cloud of related mutants rather than as a single fixed entity) (Holland 1993). That is, an RNA “virus” is really only a statistical consensus of a genetically heterogeneous population that, in turn, is in constant flux (Kilbourne 1993). This constant genomic flux permits RNA viruses to be widely adaptable to changing environmental conditions (e.g., such as shifts in the redox milieu of the host because of nutritional antioxidant activity). However, until the work of Beck and colleagues (1995) no one thought to link the nutritional status of the host with the process of viral quasispecies evolution. As discussed by Professor Domingo, nutritional deficiencies, endemic in many poorer parts of our planet, may exert an influence on the generation of viruses with altered biological properties. Such a concept is entirely in accord with our current knowledge regarding the population structure and dynamics of RNA virus populations.

Next on the program was Ernst Petersen of the University of Berne, who discussed the role of oxidants and antioxidants in viral infection and their influence not only on disease mechanisms but also on metabolic regulation (Petersen 1997). This phenomenon was illustrated by the dual role of reactive oxygen species, low levels of which are needed for cell activation but which are used for host defense by phagocytic cells at the toxic higher levels produced during the respiratory burst. The association between oxidative stress and infection was also revealed by Professor Petersen’s observation that the concentrations of several major physiological antioxidants (α-tocopherol, ascorbate and glutathione) declined during the course of infection with influenza. Noting that antioxidants probably act at several different levels, Professor Petersen called for more research on the effects of antioxidants in viral diseases, particularly when given in a blend corresponding to that found in fruits and vegetables.

The final presentation of the symposium was that of Melinda A. Beck of the University of North Carolina, who presented collaborative work showing that a benign coxsackievirus became virulent as a result of replicating in a host deficient in either vitamin E or selenium (Beck 1997). This conversion to virulence was due to a genotypic change in the benign virus and represents the first example of host diet having a direct effect on the genetic composition of a pathogen. These findings open up an entirely new way of viewing the relationship between host nutrition and resistance to infection and may well lead to a general “paradigm shift” in the field of nutrition-infection interactions.

At present, Professor Beck and colleagues simply do not know how widely applicable their results may be to other nutrient-pathogen combinations. Thus far, they have found an effect of deficiencies of two different nutritional antioxidants on the pathogenicity of one virus. A priori, however, there would seem to be no reason to exclude the possibility that other nutritional deficiencies in the host might have similar (or completely different!) effects on the evolutionary change of pathogens, especially the highly mutable RNA viruses. Likewise, there would seem to be no a priori reason to exclude the possibility that viruses other than coxsackie might be similarly (or differently) affected by a deficiency of antioxidants or other nutrients. In fact, one of our speakers (Morse) was quoted as saying “I’d be highly surprised if there weren’t others” when asked whether the evolution of other viruses might also be influenced by host diet (Manning 1996).

It would seem logical to conduct a systematic survey of various nutritional deficiencies to determine which were capable of directing the evolution of viral pathogens. By analogy with vitamin E and selenium, perhaps one could start with those additional nutrients thought to have antioxidant properties (copper, zinc, manganese, vitamin C, carotenoids, etc.) and then move on to other nutrients, deficiencies of which have previously been shown to have an effect on coxsackievirus infection, e.g., energy (Woodruff and Kilbourne 1970). It would also seem reasonable to conduct a screen of various viruses to determine which, aside from coxsackie, are affected by host nutritions. Even if limited to the closest relatives of the coxsackievirus (the Picornaviruses), one would be concerned here about the pathogens that cause polio, foot and mouth disease, and the common cold, not an inconsequential list of human and animal ailments. If the findings are applicable to RNA viruses in general, then the list of possible pathogens becomes quite long because the majority of all plant, animal and human viruses
are in fact RNA viruses (Holland 1993), e.g., measles, hepatitis, influenza and HIV, to name a few.

If this new line of research lives up to its initial promise, this interdisciplinary approach of drawing upon the combined expertise from nutrition and virology should make important contributions to our understanding of mechanisms of viral pathogenesis and provide practical information on how to maximize host resistance to infection. It is hoped that this symposium will alert workers in both fields to the advantages of such joint projects and stimulate additional productive collaborations along these lines.

LITERATURE CITED


