

A CHANGING GLOBAL ECOLOGY AND WHO ACTION AGAINST COMMUNICABLE DISEASE¹

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Communicable diseases depend on a dynamic interplay between microbial agents, the human host, and the environment. This review deals with recent changes in all three areas and how they have affected major disease patterns. Most of the author's attention is directed at environmental change.

Introduction

Ecology is a new word for many persons today. Ecology as a process, however, is as old as life itself. We are belatedly recognizing that we live in a closed biological system with a delicate balance of self-regulatory mechanisms. Until recently, man has assumed he could remain outside this system as a biological species, imposing his goals and values on nature without harming either himself or the ecosystem of which he is a part. Today this assumption is being challenged with such vigor that, indeed, it appears a "new" concept has arisen (1).

Those involved with communicable disease control have not been surprised by this "new" understanding of ecological principles (2). We have known that any communicable disease process in a population results from a dynamic interaction between microbial agent, host, and environment involving physical, biological, and social complexities. To control some diseases, only the weakest, most accessible link in the chain of causation need be broken; for others, it may be necessary to alter several ecological elements. In both cases, however, the basic concept is the same.

Today we must understand the changing balance between microbe, man, and his environment and learn to apply our public health

technology so as to alter the balance in our favor. This report reviews a few of the important new ideas, techniques, and concepts by placing them in the familiar framework of agent, host, and environment, i.e., the classical epidemiologic triangle.

The Agent

Traditional methods used against microbial agents causing disease in man have aimed to sterilize them if they are accessible outside the host, or if they are inside to inhibit their growth or kill them. The latter approach has been quite effective in controlling ancient diseases of mankind such as pneumonia, tuberculosis, malaria, and plague. However, the microbes have not been defenseless. The development of antibiotic resistance among them demonstrates a basic principle of ecological balance (3).

The most recent chapter of this fascinating story has been the discovery of "R" factor transfer between the *Enterobacteriaceae* (4). In addition to the other known mechanisms for development of drug resistance (i.e., selection by mutation, phage transduction, and direct transfer of genetic material by bacterial combination), it is now recognized that nongenetic DNA material may be transferred directly between enteric bacteria, especially the genera *Escherichia* and *Shigella*, and that this transfer confers resistance to antibiotics commonly employed against them.

We do not yet know whether the greater

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public health danger is from transfer of "R" factors between bacteria or from cross-infection of humans with resistant bacteria. Clearly, however, an entirely new problem has been introduced in the control of these enteric diseases (5).

The matter is being studied in many laboratories around the world. The World Health Organization is attempting to coordinate some of these studies on resistant bacteria, and to develop a mechanism for surveillance and rapid exchange of information concerning their emergence and distribution.

The widespread use of chemical or antibiotic prophylaxis introduces another element in the changing global ecology of microbes and men. Examples are use of penicillin for prophylaxis of streptococcal infections in patients known to have an autoimmune response producing rheumatic fever or nephritis, and administration of sulfonamides to those exposed to meningococcus. The latter procedure, however, has become the subject of increasing research and criticism.

The large number of sulfa-resistant meningococci developing during such mass prophylaxis programs has caused considerable concern. Accordingly, attention is now being focused on developing vaccines using the capsular polysaccharide antigens of the meningococcus (6). Through its meningococcal reference centers WHO furnishes information to any country requesting it, and supplies strains of meningococci with known serotypes and antibiotic resistance patterns.

Viruses remain the largest single class of microbes for which effective chemical or antibiotic agents have yet to be developed. Research now underway in laboratories in many countries will undoubtedly produce practical, effective, and inexpensive products within the next 10 years. At present, however, few have reached the commercial production stage.

The topical use of IDU (idoxuridine) against herpetic infections of the cornea stands as one of the most important developments in antiviral therapy. Investigation of its effects on systemic herpetic infections (such as herpes encephalitis

or generalized herpes infection following burns) may further extend its public health usefulness (7).

Thio-semicarbazone (Marbaran), long used as a second-choice drug against leprosy, has limited antiviral activity in smallpox. However, the drug is still experimental and has not replaced vaccination as the most effective way of preventing spread to immediate contacts.

Amantadine, developed as an antiviral agent to prevent adsorption of influenza viruses on cell walls, must be administered prior to infection, a difficult public health procedure (8). Its relative toxicity has further discouraged widespread use. Perhaps the unexpected discovery that the drug affects the course of Parkinsonism will, in the long run, be more significant than its action against influenza.

Initial enthusiasm over the possible therapeutic uses of interferon, discovered over a decade ago (9), has been revived recently by reports of interferon stimulation using non-living agents, such as polyribonucleosinic acid or polyribocytidylic acid (poly I:C) (10). These synthetic double-stranded RNA proteins seem to have the same effect as viruses in the induction of interferon. Their use in prevention and even treatment of common respiratory viral infections, such as those caused by rhinoviruses, is quite encouraging. Interferon's nonspecific viral inhibitory capacity should be extremely important in preventing multiple respiratory virus infection.

In practice, vaccines incorporating the large number of respiratory viruses (and/or many serotypes of the same virus) are not feasible. The relatively simple problem of anticipating antigenic shifts in the influenza virus, which probably has a finite number of antigens, has kept the WHO influenza surveillance network busily engaged for over 20 years. Even so, the problem of detecting a major antigenic shift in time to produce an effective vaccine and distribute it during the same influenza season has not been completely solved.

The Host

The potential for further altering host re-

sponses to infectious agents through basic immunologic mechanisms is responsible for one of the most rapidly developing fields of WHO-supported activity. The Immunology Unit, with its supporting network of reference laboratories and its own laboratory at Lausanne, has kept WHO in the vanguard of rapid advances in this field.

The unfolding story of both cell-mediated and humoral immunity has already been translated into knowledge directly applicable to communicable disease control (11). Humoral immunity to some of the killed vaccines, such as tetanus toxoid, may last 20 years or more. Further, the role of cell-mediated immunity in such diseases as leprosy, tuberculosis, brucellosis, and leishmaniasis already promises to open the way for improved understanding of their pathogenesis.

Many viruses, including attenuated vaccine strains, evoke delayed hypersensitivity to their antigens and cell-mediated immunity in host defense mechanisms. Virus-related immunopathology is therefore receiving increasing attention, and a hypothesis now links slow or latent viruses to the pathogenesis of clinical, subacute, and chronic neurological disorders. One example is the relation between subacute pansclerosing encephalitis and measles virus (12, 13). Another is the hemorrhagic fever or shock syndrome associated with an acute dengue virus infection. An immunopathologic event is thought to occur following serial infection of the same individual with two dengue serotypes. WHO-coordinated studies to test this important hypothesis are currently underway.

The recent finding that immunoglobulin A (IgA), although only a minor component of serum immunoglobulins, is the predominant immunoglobulin in external secretions has reawakened interest in the local production of antibodies along the mucous surfaces. WHO has supported several basic studies investigating the properties of this immunoglobulin, and field studies testing the ability of killed or living viruses to stimulate IgA in respiratory mucosa have already been conducted. Such studies may greatly alter immunization methods against

influenza and other respiratory viruses, if it can be shown that secretory IgA is the host's principle defense mechanism against invasion (14).

Similar studies are already investigating the importance of IgA coproantibodies against such intestinal infections as poliomyelitis and cholera (15). This newly emerging knowledge of the role of secretory antibodies in the body's defense mechanisms is likely to alter several immunization practices and policies within the next decade.

One of the oldest immunological concepts—passive antibody protection—has acquired valuable new applications. Human hyperimmune sera against tetanus and rabies have been developed, supplanting the traditional horse sera. Similarly, vaccinia immune globulin (VIG) and *herpes zoster* immune globulin (ZIG) from human sources, though rarely used, are valuable immunotherapeutic agents. The most striking development in this field has not been in communicable diseases, but in protection of Rh-negative mothers by passive administration of immunoglobulin containing anti-Rh antibodies produced in donor males.

Another large class of host-related health problems involves genetically conditioned differential susceptibility to infectious disease. An obvious example is the different response to malaria of normal persons and those carrying an abnormal hemoglobin (such as S hemoglobin) or a specific enzymatic defect (such as a deficiency of glucose-6-phosphate dehydrogenase). These cases seem to indicate a direct relation between the host's genetic structure and survival of the infectious agent, probably not mediated through the immune response.

In other instances, the relation between the infectious agent and the host's genotype (identified by classic markers such as blood groups or serum proteins) is less clear. Associations have been found between the major blood groups and smallpox, the Gc serum protein system and typhoid, and the Australia antigen and lepromatous leprosy. These associations may result from differential susceptibility conditioned by specific genotypes, or they may be

chance associations with no real biological significance.

WHO is supporting research to elucidate the relations between the agent and the host genotype in the cases of malaria and hemoglobinopathies, the Gc system and typhoid, and the Australia antigen and lepromatous leprosy.

The Environment

Environment, the third component of the epidemiologic triangle, is so complex and fast-changing that we can only give a cursory account of its importance. The changes include increasing urbanization, mass movements of man and animals in international commerce, development of virgin lands for industrial and agricultural use, and a complex of others profoundly affecting the relationship between man, his surroundings and pathogenic microbes.

Venereal Disease

One feature of such environmental change that has had an especially profound effect has been the rising incidence of venereal disease. In many parts of the world traditional restraints no longer inhibit men and women's sexual expression. Changes in life style also afford opportunity for sexual encounters, and this in turn has led to the largest known venereal disease pandemic of all time. In some countries the incidence of venereal disease is second only to that of common respiratory virus. In most countries gonorrhoea can be termed epidemic, and the expected peak of incidence has yet to be reached.

WHO is coordinating efforts to control this global pandemic by organizing international scientific seminars, promoting research on new laboratory tests for detection of gonorrhoea, stimulating the development of vaccines, and introducing international standards for treatment of cases and contacts detected by national and international surveillance programs.

Hospital Infections

The changing social and economic environ-

ment has produced a sharp increase in the availability of hospitalization for ill persons, and this has been accompanied by introduction of an entirely new medical technology. As a result, for a time it appeared that hospitals were resuming their eighteenth century role as sources of infection, rather than providing facilities for control (16).

An array of new surgical and manipulative tools and procedures have brought an increased risk of nosocomial infections. (Such new developments include organ transplants; catheterization of practically every available internal organ; and use of artificial machines to sustain respiratory, cardiac, or renal functions) (17). As a further complication, many such infections are caused by bacteria which have developed resistance to the battery of antibiotics commonly employed against them.

In addition, the patient's normal defense mechanisms are often altered by administration of immunosuppressive drugs (such as the steroids) or specific antilymphocytic sera to suppress rejection of grafted tissues. This has occasionally resulted in viremias with cytomegalovirus or herpesvirus, which otherwise would have remained latent and harmless (18, 19). And in renal dialysis units the risk of serum hepatitis has become quite substantial for both patients and staff (20). The hospital environment presents new and often unique problems in communicable disease control, which has led to the evolution of hospital epidemiology. Therefore, hospital-acquired infections should not be dismissed as inconsequential by any country developing a modern hospital service (21).

Salmonella

Many other examples could be cited of the changing role of vehicles of infection in our modern technological environment. Among the most interesting is the growing problem of salmonella serotypes spreading through countries and continents via meats, poultry, and processed foods such as bone meal, dried eggs, or milk products (22). For practical reasons, the WHO salmonella surveillance system is

presently confined to Europe, but there is need for its expansion to other areas of the world.

In Czechoslovakia during the 1930's only seven major salmonella serotypes were considered public health problems. Recently the number has increased to at least 130, of which 15 are significant. The best explanation for the difference appears to be the changing pattern of food processing within the country, and increased international trade in salmonella-contaminated products. WHO plans to increase its surveillance program, not only for salmonella but also for shigella and other causes of food-borne outbreaks.

Vector-Borne Disease

In the biological environment, the major problems requiring increasing attention from WHO are related to arthropod disease vectors, mosquitoes being the most important. However, problems related to ticks, fleas, flies, and lice also receive attention. Among the arthropod-borne diseases (malaria excepted), the vectors of dengue and yellow fever are under the most intensive surveillance and investigation. In most of the world these vectors are members of the *Stegomyia* mosquito group, of which *Aedes aegypti* is the most important species. The Vector Biology and Control Unit of WHO has an extensive computerized program devoted to mapping the occurrence and density of *Aedes aegypti* around the world, including its resistance patterns to various insecticides used in agricultural and domiciliary control (23).

Yellow fever presently seems confined within well-known zones in Africa and South America; but there is growing concern that it may be imported into receptive areas of Southeast Asia, where mosquito vectors are abundant. The recrudescence of dengue fever in the Caribbean area, once thought to be free of the problem, underlines the importance of constant surveillance in disease-free areas where the vector remains (24).

Here again, the basic problem appears to be man's changing environment. There is an ever-increasing supply of available breeding sites for

A. aegypti, such as the ubiquitous rubber tire, combined with increasingly rapid modes of travel. There is constant danger that an improperly disinfected aircraft, or an infected human travelling during the incubation period, may introduce either dengue or yellow fever into one of the world's many receptive areas.

In addition, development of irrigation systems, construction of dams, filling or dredging of estuaries, and development of large recreational areas are all producing changes in the environment which alter the relationship between man and potential arthropod disease vectors.

Fortunately, the increasing importance of arbovirus infections is balanced by the decreasing importance of some of the older, serious vector-borne diseases such as typhus, relapsing fever, and plague. Here, social and environmental changes have been disadvantageous to the vector. Unless some great social dislocation should occur in the world—with poverty, crowding, starvation, and economic deprivation reaching massive proportions—these ancient diseases should cease to be important problems (except in focal areas such as the Bolivian highlands, where typhus remains an important problem).

Tuberculosis

The changing environment has undoubtedly played a role in the gradual disappearance of tuberculosis from temperate zones over the past 100 years. Careful mathematical studies have now shown that the rate of disappearance of tuberculosis has remained unchanged over time, appearing almost independent of the control measures used (25). In accordance with the laws of probability, it seems likely to be extinguished eventually. Man's improving social, economic, and nutritional status has decreased the likelihood of transferring the bacillus to susceptible contacts and has markedly changed his susceptibility to overt disease, should such chance transfer occur. The elimination of bovine tuberculosis from man's environment has also been of importance in some countries.

Thus environmental changes have been among the major factors affecting the relationship of *M. tuberculosis* to its human host. The gradual selection of a human population with inherent resistance has also been significant, although it is less easily measured. These observations relating to the temperate regions should be useful to tropical and subtropical countries now facing epidemics of tuberculosis similar to those occurring in Europe during centuries past.

Disease Eradication and Surveillance

Among other changes in man's social environment are the emerging patterns of public health administration. The concept of eradication has been included in the administrative vocabulary of communicable disease control only within the past decade or so. Beginning with yaws, which was successfully eradicated in a few islands and isolated communities, the concept has come to include such diseases as malaria and smallpox. In the case of malaria, the rapid pursuit of eradication may have been premature, but for smallpox it seems well within the realm of practical possibility.

Although conceived several years earlier, the worldwide smallpox program of WHO was not fully implemented until 1967. Since that time there has been a 60 per cent reduction in the

incidence of reported smallpox; a continued downward trend seems assured, barring an unforeseen cessation of the program.

The elimination of urban yellow fever and dengue fever in the Americas by eradication of their vector, *A. aegypti*, has had more limited success. Man encountered a formidable foe when he confronted this species, which has successfully adapted to great ecological changes. Nevertheless, in geographically limited environments—given sufficient money, manpower, and time—*A. aegypti* can be eradicated. The problem is therefore essentially one of priorities in the competition for necessary money to accomplish the task.

Surveillance is another term increasingly used in communicable disease administration (26). In essence, WHO hopes to gradually replace the term "quarantine," including all its legalistic and prohibitive connotations, with "surveillance," meaning a scientific searching out and control of communicable diseases at their source, wherever it may be. Given the practical realities of today's world, this cannot yet be done effectively over the entire globe, so that some prohibitive regulations will be necessary for an interim period. However, as public health personnel cease being policemen and become effective surveillance scientists, a new era in the international control of communicable diseases should unfold.

SUMMARY

The object of this paper is to briefly relate WHO programs in communicable disease control to the rapidly changing human ecology of today's world. Communicable diseases are the result of a dynamic interplay between microbial agents, the human host, and man's environment. Alterations of this environment by rapid technological changes in communication, transportation, and industrialization are affecting both the types of microbes in it and man's susceptibility to them.

In general, viruses (except for smallpox and polio) and parasites have not been as successfully controlled as bacteria, mycobacteria, and

rickettsiae. Significant advances are being made in understanding alterations in human resistance or susceptibility governed by immunologic responses and genetic codes—and such understanding contributes to control.

Effective control of certain arthropod vectors has been among our more productive efforts in changing the environment. Of paramount importance is an ecological attitude which recognizes that we cannot alter one part of the system without affecting another. Our aim should be to improve the general quality of all life.

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