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CAN THE WAR TO CONTAIN INFECTIOUS DISEASE BE LOST? WITH SPECIFIC COMMENTS ON LOUSE-BORNE DISEASES[1]

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In 1965, the Surgeon General of the United States Public Health Service asked a representative group of scientists and public health administrators to review the position and activities of the United States with reference to the internationally quarantinable diseases. I was privileged to be a member of that committee, which was under the chairmanship of Dr. John M. Weir. The committee's unpublished report to the Surgeon General in 1966 focused on the "Big Six" internationally quarantinable diseases and tried to answer two serious questions: Are disease control programs based on rational scientific knowledge and progress? and, Is program perpetuation based on tradition rather than evidence of efficacy?

I would like to summarize the committee's findings as they are reflected in the current posture of the U.S. Government and changes in regulatory actions subsequently endorsed by the World Health Organization that affect us all.

Louse-borne typhus, louse-borne relapsing fever, cholera, and smallpox were no longer believed to represent major threats to the United States. This evaluation reflected confidence that introduction of these diseases into this country was unlikely and in the country's capacity to contain any introduction rapidly, and that the disease would be unable to spread in a modern American community. The other two of the "Big Six"—yellow fever and plague—were also looked on with less than alarm as they no longer appeared to represent an epidemic threat in the United States. We knew that plague was widely endemic in the western states, and that it had to be kept out of urban rat populations, and we knew how to do that. We knew of the continued endemicity of jungle yellow fever in South America and Africa, but had high confidence in the effectiveness of the yellow fever vaccine and the *Aedes aegypti* eradication programs then under way.

One outcome of these deliberations was that when a traveler enters the United States from most foreign areas, he no longer has to have a valid certificate for vaccination against smallpox, cholera, or yellow fever. Rather, he may be urged to receive such immunization before travel to an endemic or epidemic area to protect his health or because some other country requires it. In 1965, 70,000 persons were vaccinated against smallpox on arrival at our borders. This has been stopped because we know that vaccination on arrival in New York, Miami, Los Angeles, San Francisco, or other port of entry will not

[1] This paper is based largely on an earlier presentation to an audience broadly concerned with infectious diseases (*4*), and many statements herein are taken verbatim from that presentation.

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interrupt an incubation period and save the country. These steps have represented enlightened progress based on research and a fairly effective international disease reporting system, but they in no way reflect lessened desirability for the international traveler to protect himself before he travels by immunization to a number of diseases.

We have clearly won the battle and are well on the way to winning the war since the next step is to eradicate these diseases from the face of the earth. Let us take a realistic look at the probability of eradication of the "Big Six."

We are not going to eradicate yellow fever in the foreseeable future. In fact, despite our extensive knowledge and our ability to prevent yellow fever, we still observe epidemics in Africa and we may see another epidemic of classical *A. aegypti*-borne urban yellow fever in the Americas in our lifetime. This is not an unreasonable expectation in view of the work of several recent Pan American Health Organization study groups that have reviewed the current status of *A. aegypti and A. aegypti*-borne diseases in the Western Hemisphere. Three findings from their reviews emerge:

1. Yellow fever still is widely extant in South America, as is evidenced by the continued identification of human cases. These observations indicate that the jungle cycle continues in primates and mosquitoes, and that a significant proportion of persons in rural populations are not vaccinated and have contact with the jungle cycle. Indeed, there is evidence that fewer urban than rural people are immunized, so that urban human populations are quite susceptible.
2. Efforts to eradicate *A. aegypti* from the Western Hemisphere have not succeeded. Reinfestations have occurred in areas that were formerly declared clean. Many nations, including the United States, have stopped their eradication efforts for political, economic, or technical reasons.
3. An extensive area in the Caribbean, and some parts of South America must be considered receptive to urban transmission of yellow fever. This belief is based on the resurgent and recurrent series of dengue fever epidemics that have occurred from 1963 to the present. We must assume that the *A. aegypti* densities that prevail and allow the epidemic spread of dengue viruses could also support the epidemic spread of yellow fever.

One may ask how it is possible as we enter 1973 that we must concern ourselves with what we thought would be a disease that should have disappeared by this time? The problem is complex. Our research knowledge is sufficient to let us prevent the disease in human populations, but economic limitations and political priorities have come to influence disease control programs. For all practical purposes we have been told, "Sorry, we cannot let you achieve your objectives of eradicating a vector and its associated epidemic potential because economy dictates that we live with this problem."

Another problem is that the vector and a growing number of persons and organizations have exhibited resistance to the available insecticides. The vector's resistance to available products renders insecticiding ineffective or economically prohibitive, and at the same times laws are passed and social views evolve that restrict insecticide development and use. It seems clear that we will continue to live with yellow fever and that we can only hope to contain it. If an epidemic develops, it will probably be stamped out by vaccination and large-scale insecticide application, which will be expensive and cause large losses in tourism and trade.

You might say, "Well, yellow fever is the exception among the diseases listed," and you might be right. Let us not be complacent, however. In the past 10 years cholera has

spread through much of Asia, Europe, and Africa. The peoples of the Americas and Australasia are the only continental populations to escape, and the epidemic has been called pandemic or worldwide. The El Tor vibrio has demonstrated cholera's ability to resurge and the receptiveness of much of the world to the disease's reintroduction. This is a great change from 10 years ago, when we believed that advances in sanitation and vaccination had pushed cholera into its last stronghold in a limited area of Asia. We have no magic way to prevent resurgences in the future and our best hope of minimizing their impact is to develop and maintain an environment hostile to transmission. Our posture in 1973 will thus be that proposed by John Snow in his 1854 report, "On the Mode of Communication of Cholera," namely, to maintain a pure water supply and clean environment so that cholera will disappear.

We see little hope of eradicating plague since it is an enzootic infection established in much of the world's wildlife. Instead, we depend on prevention or early detection of infection in urban rodent populations. The most sobering developments with reference to plague are the finding of resistance to warfarin in both *Rattus norvegicus* and *R. rattus,* and the recognition of ambulatory carriers of pneumonic plague in Southeast Asia. If such resistance or carrier state becomes common and widespread, it will markedly affect our control efforts. For all practical purposes, public action already has taken DDT and some related insecticides out of our arsenal for flea control. Thus, we again need research developments to achieve control and good intelligence and surveillance, or we could be back trying to control epidemic plague in cities.

The best results in the war against the "Big Six" have been achieved against smallpox. The jet gun, an effective vaccine, and a dedicated corps of eradicators appear to have forced smallpox back into its last strongholds. We look forward to the World Health Organization's pronouncement that smallpox has been eradicated, but I doubt if the public will dance in the streets on that day since they take such achievements for granted; only failures attract wide attention. In the case of smallpox, the goal of eradication seems attainable if one is not completely skeptical.

Let me turn now to the diseases we will be considering here: those transmitted by lice. Few people believe that the louse-borne diseases pose a serious threat to any modern community, particularly if we assume the maintenance of our defenses, which include a functioning health agency, medical services, participation in international disease reporting, adequate water supplies, and at least adequate housing. When I discussed this problem with reference to the United States (*4*), I said: "The two louse-borne diseases still exist but seem to have retreated into a few remote areas of the world and to a constantly aging and disappearing cohort of chronic carriers in most of the formerly epidemic regions. We trust that cleanliness and freedom from lice will continue to prevail in our populations, although those of us from the 'square generation' and particularly those who are entomologists, look upon the hairdos and garb of our children and some of our elderly associates not only as a protest but also as a potential victory for the louse."

My focus today will be on louse-borne typhus in the Americas, and I will assume my comments are equally applicable to relapsing fever and trench fever, and to other geographic areas.

If one follows the *Weekly Epidemiological Reports* of the Pan American Health Organization (*3*), it is clear that louse-borne typhus is still endemic in the Americas. In 1971, 210 cases were reported from a wide area including Bolivia, Ecuador, Guatemala, and Peru. One must accept that these 210 cases were only a fraction of the actual number of cases and in no way represented the total potential reservoir in the Americas.

Any person with a history of louse-borne typhus has the potential to relapse and develop Brill-Zinsser disease (*1, 2, 5*). Such cases can be a source to infect lice. This means we are dealing with an unidentified reservoir cohort and we do not know its size, age distribution, or geographic distribution. We must assume that in areas where there is little or no active transmission, the cohort is aging, dying, and decreasing in size. In areas where active transmission continues or there is a recrudescence, new populations enter the carrier cohort. We could identify these populations by serologic surveys. We have sophisticated ways to identify and follow carrier cohorts from our studies of tuberculosis, leprosy, and typhoid fever. We have some demographic and life-table data for the populations of concern. I would hope that this meeting will direct a part of its attention to the importance of identifying and evaluating the truly endemic areas and cohorts that can develop Brill-Zinsser disease. The next step is to consider if the endemic areas or reservoir cohorts should and can be the focus of surveillance, control efforts, or cure. Acceleration of the disappearance of typhus through an attack on the human reservoir could be cheaper and more effective than another 50 to 100 years of louse epidemic control. Approaches that occur are the possibility of identifying the potential carrier cohort by serologic survey, the possible identification of future Brill-Zinsser patients if they differ from other persons in their response to antigenic stimulus, and the possibility that application of attenuated vaccines or chemotherapeutic agents to latently infected persons might decrease their chances of relapse.

We have become complacent that vector control can prevent the resurgence of louse-borne diseases and that as economic development, cleanliness, and knowledge spread the reservoir will burn out. But eradicating vectors from an endemic area would still require at least 50 years of surveillance to prevent their reintroduction, since the human reservoir cohort would persist that long. A primary purpose of this Symposium is to consider alternative approaches to louse control. This is a problem shared by many vector control programs because lice, mosquitoes, flies, triatomids, fleas, and other groups of insects and their vertebrate hosts seem capable of resisting man's efforts to control them. I believe we must assume that chlorinated hydrocarbon insecticides are on the verge of disappearing from our control arsenal, and that organophosphorus compounds will soon follow. The most effective biologic agent for killing lice that I know of is unacceptable because it is *Rickettsia prowazeki*. It is not easy to conceive of releasing a sterile or cytoplasmically incompatible population of lice to control an existing louse population. In short, economic and biologic realism may limit our efforts at control unless we are extremely innovative and convincing to the citizenries and politicians we must deal with. Mosquito control is returning to control of water and the use of larvicidal oils, and in louse control we may have to return to water, soap, and heat as our first line of defense.

It seems clear that the areas in which louse-borne typhus is endemic or populations have a significant portion of persons with a potential to become Brill-Zinsser cases are characterized by delayed economic development, restricted educational opportunities, geographic isolation, or an unfortunate history of serious disruption by war. In these areas the development and health priorities cannot necessarily be expected to include significant resources for dealing with louse-borne disease problems. Instead, the relatively unafflicted parts of the world that are concerned with the threat such diseases and situations pose must assist if the problems are to be resolved.

I would like to summarize the on-going war with what I have called the "Big Six" diseases so I can turn to some questions that

concern me. We have an encyclopedic knowledge of the causative agents and their epidemiology, and control procedures for these diseases. The generations that comprise the membership of this meeting generally adopted the concept and holy grail of disease eradication. We have not achieved our goals as we enter 1973 and the other sectors of the community who make decisions about allocation of economic resources, priorities of health programs, and legislation concerning our environment have increasingly made it obvious that their concerns and interests do not necessarily coincide with ours. The battles for knowledge through research on the classical infectious diseases were brilliantly won but are at a comparatively low ebb of funding and interest today.

In closing, I would like to add a series of questions to those posed by Dr. Snyder and that I think should concern this audience and the agencies that are sponsoring the Symposium. These questions must be resolved if we are not to have a marked decrease in the effectiveness of our control programs for louse-borne diseases and perhaps to accept that we won some short-term battles, only to lose the long-range war to abate typhus. My questions are:

1. When an epidemic occurs that requires the large-scale use of an insecticide, drug, or vaccine not licensed for use in that population, who can or will make the decision to use it and how quickly, and who will oppose the decision?
2. When an epidemic develops and the vector or pathogenic agent is resistant to the available insecticides, antibiotics, or vaccines, who will be at fault for not having monitored this and having an effective alternative at hand?
3. When the supply of a necessary vaccine, antibiotic, or insecticide is inadequate to protect a total population at risk of infection, who is at fault and who will decide the distribution pattern?
4. As private industries and, in some instances, governments withdraw from the responsibility for developing and marketing biologic and chemical agents for the control of infectious diseases, who is to assume those investment risks and social responsibilities?
5. Who is responsible when national and international resource priorities result in a scaling-down of the research establishment, health agencies, and diagnostic laboratories, and a serious epidemic results that is not quickly controlled, and emergency funds are not made available that would allow its control?
6. Are we approaching a time when a significant part of the world's society will say that the epidemics that accompany war, famine, or other social disruptions are solely the problem of the populations directly affected?

REFERENCES

1. MURRAY, E. S., et al. Brill's disease. 1. Clinical and laboratory diagnosis. *JAMA* 142:1059-66, 1950.

2. ——— and J. C. SNYDER. Brill's disease. 2. Etiology. *Am J Hyg* 53:22-32, 1951.

3. PAN AMERICAN HEALTH ORGANIZATION. *Weekly Epidemiological Report.* 44:151-53, 1972.

4. REEVES, W. C. Can the war to contain infectious diseases be lost? *Am J Trop Med Hyg* 21: 251-59, 1952.

5. SNYDER, J. C. The typhus fevers. In: T. M. Rivers and F. L. Horsfall (eds.), Viral and rickettsial infections of man, 3 ed., Philadelphia, J. B. Lippincott, 1959, chapter 42.