

Papers and Originals

Old Plagues in the Jet Age. International Aspects of Present and Future Control of Communicable Disease*

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The observation that some of the most deadly diseases of the past could in one way or another be transmitted either by man or through goods transported by ships is an ancient one. During the fourteenth century pandemic of plague (as early as 1348 in Venice, 1377 in Ragusa, and 1383 in Marseilles) ships, crews, travellers, and cargoes were being detained for 40 days: hence "quarantine," from the Italian word meaning "forty." In the absence of scientific knowledge these quarantine measures were quite naturally arbitrary. They also varied from country to country. The nineteenth century, the period of the great pandemics of cholera, saw the first attempt at international arrangements to deal with them and similar diseases. A conference convened in Paris in 1851—the first—prepared a sanitary code which never came into force. A series of conferences followed, equally unable to reach an agreement.

After the discoveries of Pasteur, Koch, and Findlay, a better scientific basis was available, and the turn of the century saw the foundation, in 1902, of the Pan American Sanitary Bureau, the adoption in 1903 of a convention in Paris, and the establishment in 1907 of the Office International d'Hygiène Publique, generally known as the "Paris Office," which led to the 1920-6 convention, completed in 1933 by a sanitary convention for aerial navigation. In 1944 the conventions were revised under the aegis of U.N.R.R.A. The aim of the conventions was to prevent the diffusion of five so-called pestilential diseases—cholera, plague, yellow fever, smallpox, and typhus—without unduly disturbing international traffic, by defining permissible quarantine measures, imposing vaccination for international travellers, disinfection and deratting of ships, aircraft, and goods, and establishing a network of mutual information. There was still a great deal of confusion. A number of conventions, some of them completely obsolete, were simultaneously in force, none of them binding on all countries.

In 1946 the constitution of W.H.O. gave that body authority to adopt international regulations, and one of the first tasks of the new organization, while still in its interim stage, was to prepare international sanitary regulations to replace the quarantine conventions of the past. Experts from all parts of the world were involved, and under the chairmanship of Dr. M. T. Morgan a special committee considered the text of the International Sanitary Regulations that were eventually adopted by the World Health Assembly in May 1951.

Air Travel

At this time air traffic was of small volume—there were fewer than four million passengers on international scheduled air services in 1948. In 1949 an aircraft still carried only 20 to 40 passengers. The speed was also moderate: in 1946

and 1947 Hong Kong to London was a five-and-a-half-day journey with compulsory night stops. At the very time the regulations were being adopted, however, the situation was changing and international travel was reaching a turning-point. The number of passengers on international scheduled airlines reached seven million in 1951, 12 million in 1955, 31 million in 1963, and 46 million in 1966. For 1967 the official figure of International Civil Aviation Organization is 51 million—more than seven times the number of passengers at the time of the adoption of the regulations—while the International Union of Official Travel Organizations reports that in the same year the number of tourists arriving by all means of transport (air, sea, and land) in 98 countries amounted to 138 million, justifying the description of the situation as the "world on the move."

The speed of air traffic also increased considerably. In 1949 the cruising speed of the fastest aircraft was 340 miles (530 km.) per hour. In 1968 it is 620 miles (1,000 km.), and it will reach approximately 1,450 miles (2,330 km.) in 1971, putting Sydney at 11 hours 20 minutes from London. The number of passengers carried in one flight has also considerably increased. After the 40 passengers of 1948 and the 70 passengers in 1950, we have now aircraft carrying 200 to 250 passengers, while late in 1969 giant "jumbo jets" will carry some 300 to 400 passengers.

Failure in Notification

We were, of course, aware that the regulations would be of value only in so far as they were adequately applied. Let us now, as objectively as possible, look at how they have worked in reality. In normal times fairly regular notifications are received in areas where certain diseases regularly occur. But when a severe outbreak of a disease occurs in a new area the system of notifications breaks down far too often. Why is this? The reason sometimes is because the disease is not recognized or takes a long time to be recognized. In more than one European country into which smallpox has been imported in the last few years notification has been made only after many secondary cases have appeared. In the recent spread of cholera of the El Tor type in the Eastern Mediterranean region more than one health administration, because they had had no experience of cholera infection for two decades or more, failed to notify the first appearance of cholera cases in their territory. Another reason is that health administrations, fearing, not without reason, excessive reactions from neighbouring or distant countries, have sometimes decided not to notify an outbreak. Early in 1967, for example, a country requested first the League of Red Cross Societies and then W.H.O. to provide supplies and vaccine to control an outbreak of louse-borne typhus which, in contravention of the regulations, they had never notified.

Another purpose of the regulations was to avoid excessive and unnecessary quarantine measures. This has also failed.

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In the case of cholera, a few years ago one country insisted that the mail should be disinfected. Three countries, one of them from Europe, requested disinfection measures to be applied to printed matter. Another country prohibited the import of tinned fruit. Trains of mineral ore were refused entry. The westbound Orient Express, with 70 passengers, was forbidden entry into a country for more than a week. Passengers on an airliner, among them the Minister of Health of India, were prevented from disembarking at an airport in one Mediterranean country and kept on board on the tarmac for many hours in the heat of a summer day. The most absurd example was that of a shipment of cholera vaccine, which remained for three days at an airport because the Iraqi aircraft sent to collect it was prevented from landing, so that other arrangements had to be made.

Thus, with regard both to notification and to maximum permissible measures the regulations are very often a dead letter just when they should be strictly applied. Let us now look at how these regulations have been effective—or not—in preventing the spread of the so-called quarantinable diseases through international traffic, and, if not, which remedies or alternatives could be suggested.

Smallpox

The intensive effort aiming at the eradication of smallpox promoted by the World Health Organization has already achieved substantial results. However, smallpox remains endemic in 27 countries in Africa, South America, and Asia. From these permanent foci of infection 80 introductions of smallpox into non-endemic countries, mostly in Europe, have been reported from 1946 to 1968. Great Britain alone has seen 32 of these, in spite of strict control over vaccination certificates for international travellers coming from infected areas. Here, and in all other countries where these introductions have taken place, it has been necessary to undertake intensive epidemiological inquiries and extensive vaccination, both costly and time-consuming for the public health services. Introduction of a single case in the United States in 1947 caused only 12 secondary cases with two deaths, but necessitated a gigantic campaign with six million vaccinations in New York City alone at a cost of several thousand dollars.

Let us speak of a specific case, now a classic, in another country. In 1963 a sailor with a vaccination certificate at the limit of its validity left his ship in Australia and flew home to Stockholm through Indonesia, India, Pakistan, and other countries. At home he stayed with his grandmother and fell ill, but only slightly, and he did not call a doctor. The grandmother also fell ill and was taken to hospital with the diagnosis of chicken-pox. The girl friend of the sailor was also slightly ill, then the sister of the girl friend and her boy friend, chicken-pox again being diagnosed. Five friends or neighbours of the grandmother fell ill, as well as the husband of one of them and two relatives. The diagnosis of smallpox was made only after 12 cases, one of them fatal, had occurred. One of the patients, who was treated in a skin diseases clinic, infected two other patients, and a chain of other cases followed—patients, nurses, hospital workers, and their relatives. Thus from the single mild case of the sailor 26 secondary cases developed and five people died.

The other introductions of smallpox into non-endemic countries more or less resemble the story of the Swedish sailor, sometimes on a smaller, sometimes on a larger scale, and often with a higher mortality. Before 1950 half of the introductions were by sea. After 1950 practically all were by air. Incidentally, contrary to the general belief, a very large majority are caused by nationals of non-endemic countries returning from travel abroad. This may well increase with the acceleration and intensification of traffic.

Obviously the international sanitary regulations have failed to prevent these introductions of smallpox, with the result that

the receptive countries have to maintain the immunity level of their population by vaccinations at a high cost: 20 million dollars annually in the United States of America, for instance.

The solution of the problem would be, of course, the elimination of the disease from its endemic foci. By the traditional method of mass vaccination campaigns it is possible, provided that a very large percentage of the whole population is covered, to suppress smallpox as a public health problem for a while. But small foci may still remain, and when in the course of the years the degree of immunity decreases in the population the disease will reappear and another mass campaign will be required. Few countries could afford the high cost of such repeated mass immunization campaigns, which are not at all necessary if proper alternative methods are applied. It is here that the essential concept of surveillance appears, as the key to eradication.

Epidemiological surveillance, from the definition of Raška used in the technical discussions at the Twenty-first World Health Assembly, can be defined as the epidemiological study of a disease as a dynamic process involving the ecology of the infectious agent, the reservoirs, and the vectors, as well as the complex mechanisms concerned in the spread of infection and the extent to which this spread will recur. Surveillance of smallpox is probably easier than of other communicable diseases, since for all practical purposes smallpox is transmitted solely from man to man, and in endemic areas its detection and recognition are comparatively simple, even retrospectively. Also there is a lapse of at least two weeks between successive generations of the disease. It has been demonstrated in some districts of India and Pakistan that a relatively elementary network of local health services can be entrusted with the task of regularly reporting on whether or not smallpox cases have occurred, provided that the staff is, as one might say, conditioned to smallpox and is all the time on the alert.

Besides this network of services providing information, only a few investigation and "containment" teams composed of adequately trained skilled health workers need to be created, to carry out investigations and when cases are detected to apply protective measures. Such a system of surveillance, in conjunction with continued vaccination of selected groups, mostly children, is much less expensive than repeated mass vaccination, and will eventually achieve the elimination of endemic smallpox without imposing on health administrations the traditional burden of repeated mass campaigns.

Cholera

Another quarantinable disease much in the news also during recent years is cholera. While in the historical focus of classical cholera along the Ganges and Brahmaputra rivers there has been a general decline in the disease during the past two decades, a new focus, this time of the El Tor biotype, which had appeared in the Celebes in 1937, suddenly spread in 1961 to neighbouring islands in Indonesia and from there swept in pandemic form to Borneo, the mainland of China, Macao, Hong Kong, the Philippines, New Guinea, Pakistan, India, Nepal, Afghanistan, Iran, the southern part of the U.S.S.R., and Iraq, and this in spite of severe, often excessive, quarantine measures. Neither vaccination—the inadequacies of which we well know—nor the other preventive measures enforced by the international sanitary regulations have been able to stop this progression, though during the present pandemic the spread has been limited so far to areas with inadequate sanitary conditions. In no country with a high standard of environmental sanitation and personal hygiene has cholera yet been able to obtain a foothold.

What can be proposed instead of the present unsuccessful system of international protection? Here again the solution would be an effective system of epidemiological surveillance both in cholera-endemic areas and in cholera-threatened

countries, but it is far from being as simple as for smallpox. Surveillance based only on clinical cases is inadequate for cholera because of what has been called the "iceberg phenomenon": the existence of many more inapparent cases and infectious carriers than of apparent cases.¹ Differential diagnosis from other acute diarrhoeas is not easy, and laboratory methods need further refinement for the detection of carriers, which still requires very unpopular practices like rectal swabs or repeated purging. No effective surveillance of cholera can be achieved without a proper reporting of all cases of diarrhoea, isolation, and treatment and laboratory facilities. All of this is obviously beyond the means of most of the countries where the disease is endemic.

In areas not yet infected but threatened by cholera—and in fact every country in the world is a threatened area—surveillance also faces difficulties. At the present rate of international traffic it is practically impossible to detect carriers, but in countries with a good sanitation and personal hygiene the risk of dissemination by non-diarrhoeic cases is minimal. However, given the modern speed of travel and the difficulty of sanitary control at airports, it is by no means impossible that a person in the incubation period should arrive, for instance, in a country of Western Europe and present with a highly contagious acute form of cholera. An outbreak could easily occur in communities living in poor sanitary conditions. Even when the sanitary conditions are better, as is shown by the typhoid outbreak at Zermatt, in Switzerland, an unprotected water supply could, through a series of unfortunate coincidences, be contaminated by pathogenic organisms and spread the disease. Remote as such a possibility may be, it should be kept in mind.

Yellow Fever

Yellow fever could also present a formidable problem. In the past yellow fever has occasionally invaded North America and Southern Europe from its original foci in tropical Africa and tropical America. During the present decade severe epidemics have broken out in Africa. Some 30,000 deaths have occurred in Ethiopia, with *Aedes simpsoni* as the vector. In Senegal in 1965 several hundred deaths were caused by the disease, this time transmitted by *Aedes aegypti*. Last year yellow fever appeared on the Liberia-Ghana border.

In tropical America efforts towards the eradication of *A. aegypti* have reduced the risk of outbreak of the urban type, but last year an outbreak of the jungle type was reported in north-west Argentina, near the Brazil border. Both in Africa and in America the disease will persist in the jungle form, with monkeys as a reservoir and treetop-breeding mosquitoes as vectors that could transmit the disease to man. True, the international regulations provide for the compulsory vaccination of travellers going from infected areas to receptive zones, but in spite of the nearly total efficacy of the vaccine it does not provide absolute certainty of protection. The same applies to disinsectization of aircraft, which is compulsory but apt to be ineffective. With the speed of travel at present, and even more with the speed of travel of tomorrow, a traveller infected in the forests of Brazil, for instance, could reach a south-east Asia town well within the incubation period. There, theoretically, the virus would find ideal climatic conditions, an unvaccinated human population, and its favourite vector, *A. aegypti*. Until now yellow fever has never been introduced into Asia, and this is an epidemiological mystery, but the possibility of its introduction can by no means be excluded.

Thus surveillance in both endemic and receptive areas is essential. In endemic countries it means continuing clinical and pathological surveillance, a continuing study of the natural foci, as well as the mapping of *A. aegypti* populations.

¹ See, in particular, A. M. Kamal, *Bull. Wld Hlth Org.*, 1963, 28, 284.

Other Quarantinable Diseases

The other so-called quarantinable diseases are of relatively less importance from the point of view of international transmission.

Plague continues to exist in wild rodents in Asia, Africa, and America, and outbreaks of urban plague have occurred recently in a number of countries in these continents, with the classical big increase in incidence in Vietnam owing to war conditions. There is always a potential risk of international transmission by rodents, mostly rats, by ships, or even by large cargo planes, though no such occurrence has been reported for many years. The provisions of the regulations for rat-proofing, deratting, and disinsecting of ships, and, if required, of aircraft are the best protection against plague, if associated with a continuing surveillance of the rat population in harbours and, if needed, in airports. Continuing surveillance of natural foci of wild rodents plague is of course important. The risk of transmission of plague by man is very remote and practically negligible.

Louse-borne typhus and louse-borne relapsing fever persist in small and restricted foci, of both in Africa, and of typhus in America and Asia. Their transmission through international traffic is very unlikely, and in fact, though a very few cases of typhus being introduced have been reported, no outbreak has ever followed. This, of course, does not mean that these diseases should not be the subject of active measures against lice in their endemic foci.

"Non-quarantinable" Diseases

Many other diseases not considered as "quarantinable" are nevertheless apt to be transmitted internationally.

Influenza, for instance, though it produces large-scale pandemics, sometimes with a high mortality and always with serious effects on the economy, is not dealt with in the regulations. Internationally the problem of influenza has been approached in a different way through a programme set up by W.H.O. many years ago, even before it became a permanent agency. Sir Christopher Andrewes was among the first to express the need for such a surveillance programme, and his laboratory in London was designated as the World Influenza Centre in 1947. Now 79 national influenza centres in 54 countries collaborate in the programme, the objectives of which are to collect and disseminate information on the occurrence of influenza and on the antigenic structure of the current virus. This is most important, since, as we all know, this structure changes at intervals.

The programme has been given an opportunity of showing its efficiency in the recent emergence of a variant of the A2 strain which differs greatly from the previous ones. It first attracted attention in early July, when an epidemic of about 500,000 cases occurred in Hong Kong. Even before the epidemic had reached its peak the strain had been isolated by the influenza centre there and flown to the world centre, where within two weeks it was characterized, freeze-dried, and made available to research workers and to vaccine production laboratories. The epidemic, as expected, is pursuing its course. It is important to stress once again that this programme is outside the international regulations and is based on voluntary collaboration between a number of laboratories in many countries. Its activities—the detection and identification of variants and the isolation and distribution of strains—are conducted on a scientific and professional level and contain no elements of compulsion or regulation.

Typhoid and salmonellosis of many types can be introduced by infected persons, by meat and meat products, which are more and more transported across the world in cargo planes, and by the food and drinks available in passenger planes.

Diphtheria and whooping-cough, well under control in highly developed countries, are still prevalent in developing

countries. There is a risk of the reintroduction of both where the systematic vaccination of children is neglected, leaving the child population unprotected, and, in addition, of the introduction of whooping-cough strains that are immunologically different from those against which the children in developed countries are protected.

Among vector-borne diseases, other than the ones that are quarantinable, there is the vast group of arbovirus infections, some of which have attained epidemic proportions in the recent past. For instance, the dengue-type viruses, responsible for highly fatal haemorrhagic syndromes, or the equine encephalitis of the Americas pose a potentially serious problem where the appropriate vectors exist.

Malaria

Among the vector-borne diseases malaria deserves the greatest attention because of the danger of its reintroduction into countries that have been freed from the disease. The risk until now has been minimal, for most of the areas where malaria eradication has been achieved are in temperate climates, the transmission potential there is low, and the health services are well developed. The risk is much more serious in tropical areas, where the transmission potential is high and the health services are inadequate. Malaria is being eradicated by way of elimination of the malaria parasite through the interruption of transmission, but the mosquito vector is still present. Reintroduction through infected mosquitoes or through persons carrying the malaria parasite, if not immediately detected and checked, would jeopardize the results achieved by long-lasting and highly expensive eradication campaigns. The reintroduction of infected mosquitoes can be prevented by the disinsection of aircraft and the elimination of mosquitoes from airports and surrounding areas. To prevent its introduction by persons carrying malaria parasites in their blood is far more difficult. The requirement of a blood examination for every traveller from malaria-infected areas would be a reasonably effective measure, but it faces obvious practical difficulties. The only solution is an efficient system of surveillance of recurrence or reintroduction of malaria where it has been eradicated.

Regulations Inadequate

It seems evident that the system of protection based on the existing international sanitary regulations is no longer adequate. No doubt the regulations have been useful in promoting some degree of international co-operation and in establishing a network of data collection and disease notification which, though incomplete and often unreliable, has been a definite step in advance. Nevertheless, in this jet age, with the appearance of subsonic—and soon supersonic—aircraft of a speed and size unthought of 15 years ago, and with the prodigiously increasing number of international travellers, a thorough and unbiased examination of the causes of failure of the present system and the possible remedies is not only timely but long overdue.

The failures are basically caused by the lack of accurate reporting, owing to faulty systems of detection, but—let us be frank about it—even more to the lack of sincerity on the part of the national health administrations. Why this lack of sincerity? There is national pride, there are internal political factors, but above all there is the fear of the irrational and excessive quarantine measures other countries would apply, of which we have seen many examples. In turn, the knowledge that most of the infected countries hide or minimize the facts leads to a reinforcement of these irrational quarantine measures. This vicious circle should be broken. Its origin is to be found in the now outdated character of the general approach to international protection.

International health policies are still founded on a defensive and a negative attitude. They have an inherent element of compulsion, a police aspect, which is expressed in the very word “quarantine” or, in French, “police sanitaire.” The police action at the national level is usually entrusted to distinct administrative entities such as “quarantine bureaux,” “contrôle sanitaire aux frontières,” often separate (though that is not the case in this country) from the epidemiological services and the network of public health laboratories. Internationally, the same separation was expressed in the World Health Organization by the existence of a distinct unit labelled “International Quarantine.” This police-like administrative structure and the negative policy which it applies induce the feeling that the so-called pestilential or quarantinable diseases are a sort of sin that spoils the national image and so should be hidden away or played down to the greatest possible extent. The time has now come to take a more scientific, objective, and positive attitude towards all communicable diseases, whether or not they belong to the ancient group of the shameful pestilences.

International Responsibility

Survey, detection, recording, and notification of all communicable diseases should be the responsibility of an integrated epidemiological surveillance service, itself part of the general health services of the country and benefiting from the facilities of the national network of public health laboratories. A natural extension of such national responsibility of the surveillance services would be international responsibility, including early notification, as well as measures preventing the export or import of communicable diseases. Gradually better understanding and more sincere co-operation would develop between the national epidemiological services of the various countries and confidence would be restored. As a symbolic gesture, but also as a means of improving the efficiency and quality of services offered to its member States, W.H.O. has decided to merge its time-honoured unit of International Quarantine with the more recently established unit of Global Epidemiological Surveillance. This merger definitely emphasizes the pre-eminence of a scientific and technical approach as opposed to a legalistic and regulation-minded approach, both nationally and internationally. The influenza programme has shown us a good example of what it is possible to achieve efficiently at the scientific and professional level. Let us hope that in the course of time this trend will become general.

Meanwhile the international sanitary regulations will certainly continue to be enforced, but with gradual improvement. Some of us may have believed in 1951 that they provided a more or less definitive solution, but such unconditional optimism was not general.

Conclusion

It is a platitude nowadays to refer to the increasing gap between the developed and the underdeveloped or developing countries. Platitude or not, this is one of the tragic features of our times. The only method of filling this gap is to increase in a very large measure the economic and technical assistance given to the less-favoured countries. Allow me, therefore, to conclude that, in this age of jet planes and soon of supersonic transport, the only way of preventing the old plagues, and some new ones, from spreading from continent to continent and from country to country is to help the poorest nations of the world to reach such a level of economic and technical development that it will be possible for them to combat the evil at its source.