tems, provided that the direction of time in the equations is reversed. Since Schmidt made this suggestion, active work by a number of Russian astronomers (*9*) has done much to clarify the problem of capture. Direct numerical integration shows a possibility of capture, and general inequalities on initial conditions have been formulated indicating the conditions under which capture can take place. There has not been an application of these general results to the problem of the earth-moon system.

Observational Determination of the Nature of the Moon's Interior

A number of straightforward observations would do much to reduce the present uncertainty as to the nature of the moon's interior and the past history of the moon. The placing in orbit of a lunar orbiting satellite and the detailed trackings of the satellite would provide critical information on the ratio $C-A/Ma^2$, and this, combined with data on the inclination of the axis of rotation of the moon, would determine the mean moment of inertia. A knowledge of the mean moment of inertia fixes the degree of differentiation of the moon and provides data of a fundamental character for the investigation of specific lunar models. This observation is perhaps the most critical of all, since it gives an immediate measure of the bulk properties of the lunar interior.

Seismic observations of various kinds will also yield valuable information. Measurement of the level of natural seismic disturbances will provide a means for estimating the current release of thermal strain energy. A network of seismic stations can be used to obtain a detailed description of the variation of elastic-wave velocity with depth.

The measurement of the surface heat flow involves the concurrent measurement of the near-surface temperature gradient and the thermal conductivity of the surface material. The surface heat flow can lead to estimates of the present thermal state of the moon. In combination with measurements of the radioactivity of the moon, measurement of the heat flow can provide theoretical limits for the initial thermal state of the moon.

The placing of a tidal gravimeter on the surface of the moon will permit measurement of the tides raised on the moon by the gravitational action of the earth. In addition to the variation of gravity due to the direct actions of the earth (and of the sun), there is a variation resulting from the elastic distortion of the moon. The amplitude of this distortion determines the bulk elasticity of the moon, while the phase lag of the displacements fixes the anelastic properties of lunar matter.

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Eradication of Infectious Diseases

"Control" is an unending operation. After "eradication," no further effort is required.

T. Aidan Cockburn

"Eradication" of infectious disease as a concept in public health has been advanced only within the past two decades, yet it is replacing "control" as an objective. The meaning of the term varies with the user, and the difficulties of achieving eradication, in any form, are usually underestimated. In this article (*1*) my own definition of eradication is offered, the difficulties common to all schemes of eradication are discussed, the significance of animal parasites in this connection is outlined, and brief comments are offered on selected eradication schemes.

Definition

In my definition, eradication is the extinction of the pathogen that causes the infectious disease in question; so long as a single member of the species survives, then eradication has not been accomplished. The definition implies action on a world-wide scale, but world eradication has not yet been achieved for any infection. "Regional eradication" implies a basically unstable situation, because at any time the infection may be reintroduced by carriers or vectors from outside. The occurrence of occasional small episodes of infection in a cleared area does not invalidate the claim that regional eradication has been achieved in that area, provided the infection was imported. For areas where vectors are present but without the parasite, one may still claim eradication—as, for example, in Sardinia where there are anopheles without the *Plasmodium*, and in the United States where there are *Aedes aegypti* without the yellow fever virus. In South America, yellow fever virus cannot be eradicated, since it is endemic in the monkey population of the forest; however, eradication of the domestic vector *A. aegypti* from the continent is under way, and this situ-

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ation could be defined as "urban" eradication of yellow fever, and "regional" eradication of the mosquito.

Even if world-wide eradication of an infection is achieved, there is the possibility that a similar infection may evolve from related organisms still existing in nature after measures of eradication have been halted.

There is an essential difference between the concepts of eradication and control. Once eradication is achieved, the infection is gone forever, and the costly burden of recurring control measures may be dropped. Eradication can, therefore, be regarded as that state in which the infection does not return from infected areas after control measures have been abandoned. If procedures have to be continued to prevent return of the infection, then the state is one of control and not eradication.

Some pathogens persist in the body for long periods of time, and, strictly speaking, eradication has not been accomplished until the last parasite has died. However, in regional eradication, the practical definition can be used, and each infection can be judged independently. For example, in Brill's disease the rickettsiae persist in the body for very many years; in the United States, there must be people who became infected abroad and who are still carrying the pathogen, yet the infection must not be regarded as established here, since the chances of transmission are remote. Similarly, in malaria the parasite can persist in the body for years; many people in the United States are infected, but because the likelihood of transmission is very small, even without control measures, eradication can be claimed. The situation is different in an area where conditions favor the transmission of malaria; should eradication measures based on mosquito control be abandoned while the parasite still persists in the human host, then, even though the disease has not been reported for some time, there is a possibility of a recurrence of transmission, and the claim of eradication is not justified. In world eradication programs, the strictest adherence to the definition should be maintained; thus, in the case of smallpox virus, which can live for many months on infected clothing, a time allowance on this scale should be made after all other signs of the infection have disappeared. In malaria, before eradication as defined here can be claimed, there must be many years' surveillance after the last case has been diagnosed.

The definition given above is in general agreement with the World Health Organization's definition for malaria eradication. In its original form the World Health Organization definition was interpreted (*2*) as meaning "the ending of the transmission of malaria and the elimination of the reservoir of infective cases in a campaign limited in time and carried to such a degree of perfection that, when it comes to an end, there is no resumption of transmission." The criteria of malaria eradication to be adopted included adequately demonstrated absence of transmission and endemicity for a period of at least three years, in at least the last two of which no specific general measures of anopheline control and no routine chemtherapy had been applied (*3*). The World Health Organization definition was modified still further to give more precision to the surveillance requirements (*4*), but it still does not go so far as to include the final elimination of the last parasite and does not mention related infections in animals or the theoretical possibility that the infection may evolve again.

History

Deliberate attempts to stamp out infectious diseases began in the closing years of the last century. In 1892, an animal infection, contagious pleuropneumonia of cattle, was declared eradicated from the United States after a campaign that lasted five years and cost nearly two million dollars (*5*). In England, in 1896, rabies was eradicated successfully by enforcing a muzzling order for all dogs for one year and enforcing a six months' quarantine for all dogs and cats. In 1917, the decision was made to eradicate bovine tuberculosis in the United States, under the Federal-State Cooperative Plan for Eradication of Bovine Tuberculosis. The program called for the testing of all cattle in the United States and the killing of the reactors, and it was extremely costly both in money and in animals. The campaign was not pushed to the extreme required for eradication, and it was unsuccessful in that bovine tuberculosis still exists in this country (*5*). Yellow fever was eliminated from Cuba in the first decade of this century by antimosquito measures, and this gave rise to such high hopes that in 1914 Gorgas could state that world eradication of the disease not only was practical but could be achieved at a reasonable cost (*6*). With the discovery of forest yellow fever, these hopes were disappointed and the idea of eradication was discredited.

Modern ideas on eradication begin with the work of Soper and his colleagues in South America. In 1930, some dangerous African mosquitoes, *Anopheles gambiae*, were discovered in Brazil by Shannon, and in a few years these had spread and were the vectors responsible for a disastrous epidemic of malaria in the northeast section of the country. A program to eradicate every single specimen was begun in 1939, and by 1941 the task had been completed (*7*). Side by side with this program, the control of *Aedes aegypti* mosquitoes had progressed so well that in 1942 Soper was encouraged to propose eradication instead of control. The following year, Bolivia was the first country to proclaim that this goal had been reached (*6*). Since that time the countries of South America have joined forces, aiming for complete continental eradication. By 1959, substantial areas had been cleared (*8*) (Fig. 1).

These successes with mosquito eradication made *eradication* a respectable term once more, so that world eradication of smallpox and malaria are now proclaimed aims of the World Health Organization, in programs supported by many countries and backed financially by the United States. At present, eradication is described as the aim in many other infectious-disease projects.

Basic Program Needs

All eradication programs have many needs in common. These include the need for political stability, for popular support, for adequate organization, for logistic and technical backing, and usually for an efficient quarantine system to prevent reinfection of the cleared area. Most important of all, the efforts must be pushed to the limit until the last parasite has been eliminated. The last 5 percent is as important as the first 95 percent. Anything less than 100 percent is not eradication.

Political stability. Eradication programs are usually long-term, often requiring international cooperation. Obviously, nations work together better if they are at peace and friendly. Political upheaval and war usually disrupt such projects, and in countries like Tibet, where fighting is in progress, eradication programs are not likely to succeed. However, the recent collaboration of so many countries on issues such as malaria and smallpox has shown that much can be done even in a troubled world.

Popular support. Obviously, a program of eradication, with all its costs and inconvenience, will not be successful if it does not have popular support, even in a small country. On a world scale, this task of insuring popular support might well daunt the most fervid supporter of the principle were it not for the United Nations. It is only through the United Nations that the two programs of smallpox and malaria control have been adopted by the majority of people, and even then it is clear that some of the nations involved have only a lukewarm interest in the project, while mainland China, biggest of all countries, with its 600 million people, is not even in the United Nations.

Great difficulty arises in areas where an infection of global or continental significance is of no particular public health importance locally. It is difficult to persuade a community to put up the funds and make the effort required for something that causes little local inconvenience. For example, a few countries joined in malaria eradication only after some hesitation; for them, malaria was simply not a public health problem, and there was no public pressure to organize expensive measures to benefit neighboring countries.

The costly and time-consuming efforts made to eradicate *Aedes aegypti* mosquitoes in urban areas have been substantially successful in South America (*8*), but as there is no yellow fever in the United States, there is no public pressure to get rid of *Aedes aegypti* mosquitoes there (Fig. 1). None the less, the United States has an international obligation to eradicate this species of mosquito, for its representatives supported and voted for the resolution in the first meeting of the Directing Council of the Pan American Sanitary Organization, a meeting in which it was resolved that *Aedes aegypti* mosquitoes must be eradicated from the Americas (*9*). As long as there are *Aedes aegypti* mosquitoes in North America, there will always be a likelihood that they will reinfect the areas in South America that have been cleared.

Syphilis might be eradicated from the United States by means of antibiotics and technical services already available, but it is unlikely that the public would accept an eradication program.

Technology. Eradication in any particular country may be impractical because the government lacks the funds or the personnel or the equipment or the organization. In certain nations of Africa, Southeast Asia, and other parts of the tropics, the number of physicians and other trained personnel may be too small even for routine tasks, let alone the difficult and burdensome techniques of eradication. When the total national budget is inadequate, the proportion allotted for health purposes is usually small.

Equipment may be scarce, not to mention spare parts and repair technicians. Transport is frequently difficult because of a scarcity of vehicles and drivers and even of passable roads. For eradication it is not enough to reach most places; one must reach all places. Usually 95 percent are reasonably accessible, but the remaining 5 percent are equally important.

The administrative organization of the national health department in the country undertaking eradication procedures must be strong enough to take the load. Usually, in underdeveloped countries, the department is so small that one man does work that should be done by ten. Frequently major duties are left to clerks, since no one else is available. To expect these overworked people to take on responsibility for a large additional program is to be overoptimistic.

It might be expected that foreign aid would supply the needed technicians, administrators, equipment, and supplies. This it can do to a large extent, but there is a crucial service that can be performed only by the host nation itself. For example, the first stages of a program are usually easy enough, with teams of workers, imported or trained by foreign technicians, spraying the countryside with insecticides, giving injections or vaccinations, or handing out pills, and with everyone pleased as the disease in question recedes. But when the foreign teams depart, the task of finishing the job and of continuing surveillance falls to the host government. Then the government needs an efficient health service, with trained doctors who, in the course of their duties, will spot and report any recurrence of the disease. This program of surveillance has to be carried on for years in order that recurrences may be promptly discovered and stamped out in time. This task may be beyond the scope of any foreign aid, and all too often the national health department simply cannot carry it out. The final results over a ten-year period might well be especially disappointing if the program had started off well.

Reintroduction of a pathogen is an obvious danger where the operation is limited to a country or a continent, with infection remaining in regions outside. The usual method is to enforce quarantine measures, but the volume and nature of travel nowadays, especially by air, is making quarantine increasingly ineffective.

Biologic Factors in Eradication

On the basis of modern evolutionary theory it may be assumed that all human infections are derived from ancestral animal infections, since man himself was once a nonhuman animal. *All* human infections have related pathogens still existing in animal hosts, and the nature of these animal pathogens to a large extent decides whether or not an infection can be eradicated. Man belongs to the order Primates, and his relations the apes, the monkeys, and other primates share with him parasites that have been handed from one generation to another from their common primate ancestor. Elsewhere it has been suggested that these parasites include the intestinal protozoa, pinworms, herpes virus, malaria parasites, and so on (*10*, theory 2). In addition, there is a sharing of parasites among animals in intimate contact in the same ecology, as, for example, between man and his domestic animals. Sometimes this sharing is continued without change in the form of the parasite, and a new form of zoonoses is established, while in other instances a newly parasitized species of host will convey the parasite within its own population and in time a new strain will be selected that is largely specific to that host. Elsewhere it has been suggested that this is the way in which the pox viruses evolved among the animals brought together into man's ecology when man settled down and domesticated animals (*10*, theory 6).

Some of these relationships are close indeed; others are not so close, and some are fairly distant. When any eradication of an infection is contemplated, it is essential that the evolution of the agent be studied to determine the nature of these relationships and the effect they will have on the final result of the program. Related animal infections can be grouped as follows.

1) *Identical.* These infections are the zoonoses. From the point of view of eradication they can be subdivided into infections of wild animals and infections of domestic animals. If wild animals are involved (as in rabies, yellow fever, plague, rickettsial infections, or salmonella infections), then eradication will be difficult if not impossible. If only domestic animals are involved (as in *Mycobacterium bovis* infections, brucellosis, and glanders), then "regional" eradication is easy, for all that is necessary is to test the animals and kill the reactors, or else immunize the stock. However, research may show that most infections in domestic animals occur also in wild animals, and that world eradication may be impossible.

2) *Closely related.* In nature, closely related species sharing the same ecologies compete with one another, and this must happen with parasites also. Possibly the distribution of each species is to a certain extent dependent on this interspecific competition. A zoonosis like yellow fever is related to a wide range of other arbor viruses and almost certainly is affected by them. This is the explanation sometimes proposed for the absence of yellow fever in India, where the facilities for spreading have existed for at least 2000 years. If yellow fever virus were completely eradicated from Africa, it might well

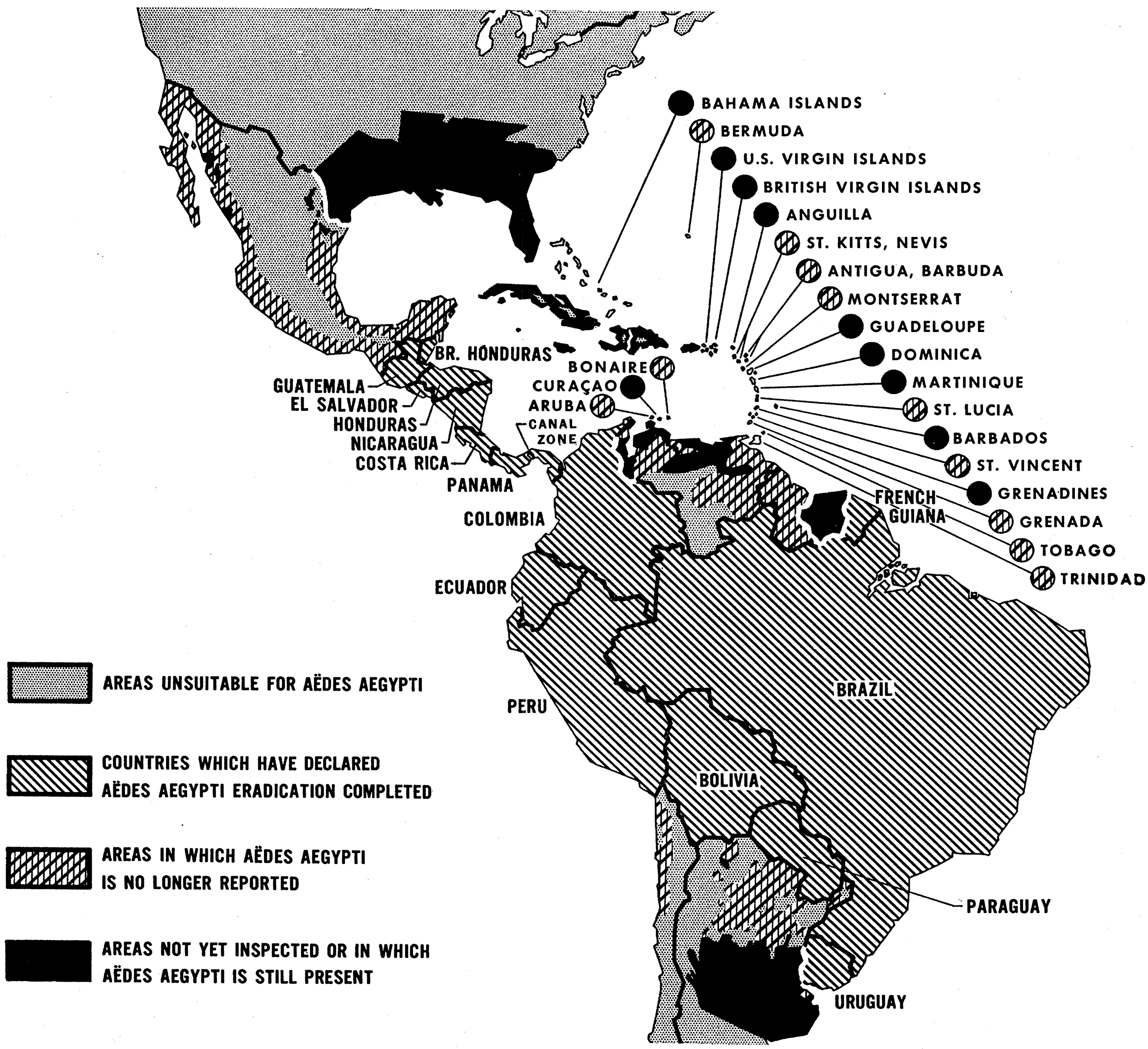

Fig. 1. Status of the *Aedes aegypti* eradication campaign in the Western Hemisphere in December 1960. "*Aedes aegypti* eradication completed" signifies that eradication has been verified in accordance with the standards established by the Pan American Sanitary Bureau. [Pan American Health Organization]

be that related, competing viruses would emerge prominently in that area.

Parasites similar to malaria parasites of man exist in apes and monkeys. The question as to whether they are identical is a matter of urgent research at the moment, but in any event there is no question but that man can be infected with these parasites (*4*). Should the human malaria parasites be eradicated but not the vectors, then, after the eradication measures had been halted, man would be reinfected from the primates, if these have identical parasites, or if they have not, over a period of decades human parasites might re-evolve from parasites of the primate reservoirs. In either case, human malaria would be likely to reappear.

As to treponemal infections, the various species are probably mere variants of one basic organism (*11*). Interspecific competition may partially determine whether a population contracts yaws or syphilis. Eradication of yaws will probably result in an increase in syphilis.

3) *Substantially different.* An infection such as smallpox is closely related to infections in other animals in man's immediate ecology—animals such as mice, cows, horses, sheep, or chickens. It is possible that all of these infections derive from a radiation of a single organism that occurred at the time man first settled down and domesticated animals (*10*, theory 6). These organisms are now so highly adapted to their hosts, and conditions have so changed from those under which they evolved, that the possibility that smallpox would re-evolve appears to be remote. The chances, therefore, of permanent eradication of the infection seem good.

4) *Very remote relationships.* Organisms like the leprosy bacillus have probably been symbiotes of man and his predecessors over many millions of years, are closely adapted to man, and have no close relations in other animals. Once eradicated, the chance of their re-evolving is extremely small.

It is becoming increasingly recognized that an organism that has radiated into many species is more capable biologically of surviving than one which has only a few species (*12*). A large organismal group is well equipped to withstand the adversities of changing environments and to adapt to new conditions as they arise. This strength arises from the variety of genetic mechanisms present in the radiation, in contrast to the limited range of mechanisms for organismal groups with only a few species. In general, wide radiations are found mainly in the locations of origin of the ancestral organism, and only single species or narrow radiations are found in areas where the organism has been newly introduced, for it takes considerable time for new species to appear. Eradication procedures will therefore be easier to complete and more successful, in long-term effects, when employed against species of parasite or insect vector that have colonized the area in recent times than when employed against species that have been established there perhaps for millions of years.

The program to eradicate *Anopheles gambiae* in Brazil was a success, possibly because the mosquito was an introduced species, while a similar program against *A. labranchiae* in Sardinia was a failure in the sense that the mosquito species was not completely eliminated, because the anopheles in Sardinia were indigenous to the island and probably had been there many thousands or even millions of years (*13*). In addition to the mosquitoes which have become adapted to feeding on man within recent times, there was the original native stock, still feeding on wild animals. These mosquitoes of the original stock were not greatly affected by the eradication program and, presumably, form a reservoir from which fresh strains of domestic mosquitoes will evolve now that the program has terminated. Similarly, eradication of *Aedes aegypti* is proceeding very well in South America, where it probably is a newcomer of only some 400 years' standing, and where wild strains in the forest are as yet unknown. The story would be different should a similar program be attempted in East Africa, where wild strains are well established in the forest.

It is sometimes said that when an organism has been reduced to very small numbers it cannot survive and will die out spontaneously. This idea is of practical importance in eradication programs, for the last few sources of infection are difficult to reach. It is probably often true as applied to animals that are genetically diploid, but not necessarily so with microorganisms that are haploid. For example, the whooping cranes are probably doomed to extinction merely because there are only about 40 of them left alive. Deleterious or lethal mutations will occur occasionally in them; since most will be recessive, those that do not result in death will be stored away without expressing themselves. The close inbreeding that occurs in so small a population as 40 will result in these recessive deleterious mutations becoming demonstrated in the phenotype, so that the birds will become increasingly unfit to survive. They will be saved only if the environment changes substantially in their favor.

With haploid organisms, this is not the case, for any mutation is likely to be expressed immediately in the phenotype, and if the mutation is sufficiently deleterious, the individual organism will fail to survive. The future population of the haploid organism will consist only of the descendants of those without the mutation, so that small numbers do not necessarily indicate that the population is doomed to become extinct.

In a vector-borne infection, the pathogen will die out if the density of the vector is too low. This is a well-recognized phenomenon in malaria, yellow fever, plague, and filaria, and usually in control programs there are indices, such as the *aegypti* or the *cheopis* indices, of the permissible levels of vector densities for control of the infections. Should the numbers of these vectors be kept permanently below the threshold levels, then in time the pathogens will be eradicated. However, in any large country there may be small local pockets where high density levels of the vectors may persist, even though the general level for the area is low, and in an eradication program these must be sought for diligently. These pockets will not be so important in an infection like yellow fever, where the infectious process in the host is brief and the host population soon becomes immune to the pathogen, but they can be extremely important in malaria and filaria, where the host can carry the parasites for years.

Certain infections have been known to dwindle to small numbers and then disappear spontaneously. The extinction, however, was not due to the parasite population's falling below a hypothetical numerical threshold but to the parasites' having lost their fitness to survive in the environment. "Fitness" can be defined as an organism's capacity to produce regularly as many viable members in one generation as in the preceding generation, for if it produces fewer in each succeeding generation it will become extinct. Changes in environment and in behavior in places such as England and the United States in the past hundred years have tipped the balance against many parasites such as lice, the malaria parasite, the cholera vibrio, bubonic plague bacilli, and tubercle bacilli, and these infections, if they have not completely disappeared, are becoming less and less frequent. This process is clearly due to environmental changes and not to mere smallness in numbers of the parasites; the paucity of the organisms in the closing stages is merely the final step in a continuing process.

In a country where conditions favor the parasite, the elimination of this last trace of the infection can be extremely troublesome; yet until it has been accomplished, the campaign will not be a success. If the operating procedures are stopped prematurely, the infection will return, and either the program will have to be recommenced or else all the effort will have been wasted. In Ceylon, antimosquito measures were commenced in 1945 with the then newly available residual insecticide DDT, and the results exceeded expectations, for within one year there had been a dramatic fall in the incidence of malaria. After a while the general spraying was stopped because of the increasing resistance of the mosquitoes, and reliance was placed on a surveillance system, with spraying of local infected areas. However, the malaria did not dwindle and vanish as expected but continued, and at the end of ten years it was still present in certain small foci (*14*). Malaria had been controlled but not eradicated. More vigorous measures are now being taken to discover and deal with these small foci.

The story has been much the same in Haiti, where yaws eradication is being attempted (Fig. 2). There had been 45,356 cases of yaws reported in 1949 in the island; in 1950 the general population had been given penicillin, and in 1953 only about 400 cases of yaws could be found. Every year since then the program has continued, and the early eradication of yaws has been eagerly expected, but each year up to 1959 there continued to be a hard core of about 300 cases (*8, 15*). In nearby Jamaica, the yaws eradication program had made considerable progress when the teams for checking and surveillance were withdrawn prematurely. In 1959, 415 new cases of infectious yaws were reported, and the program is to be resumed (*8*).

This kind of experience underlines the difficulties in the later stages of an eradication program. Once the first enthusiasm for the program has dwindled and the disease to a large extent has disappeared, it is difficult to keep the teams in the field and at a high level of efficiency. The mode of transmission may be difficult to see, so that cases pop up in unexpected places, and often supreme efforts are necessary to bring the transmitting agent to light. Soper has called this level of infectivity the "threshold of visibility" below which the mode of transmission of the infection cannot be seen with routine methods (*16*), and it is this that causes campaigns to drag on year after year when, according to all expectations, they should have been completed.

Eradication in Practice

Small islands are obviously the places where eradication efforts can best be made, for there the problems are clear-cut and quarantine measures are easiest to enforce. In England, several infections have been deliberately eliminated, including smallpox, rabies, and glanders, while typhus, plague, relapsing fever, malaria, cholera, and possibly leprosy have vanished, probably as a result of changing environments and habits. Smallpox was everywhere in England in the 18th century, but in 1867 vaccination was made compulsory.

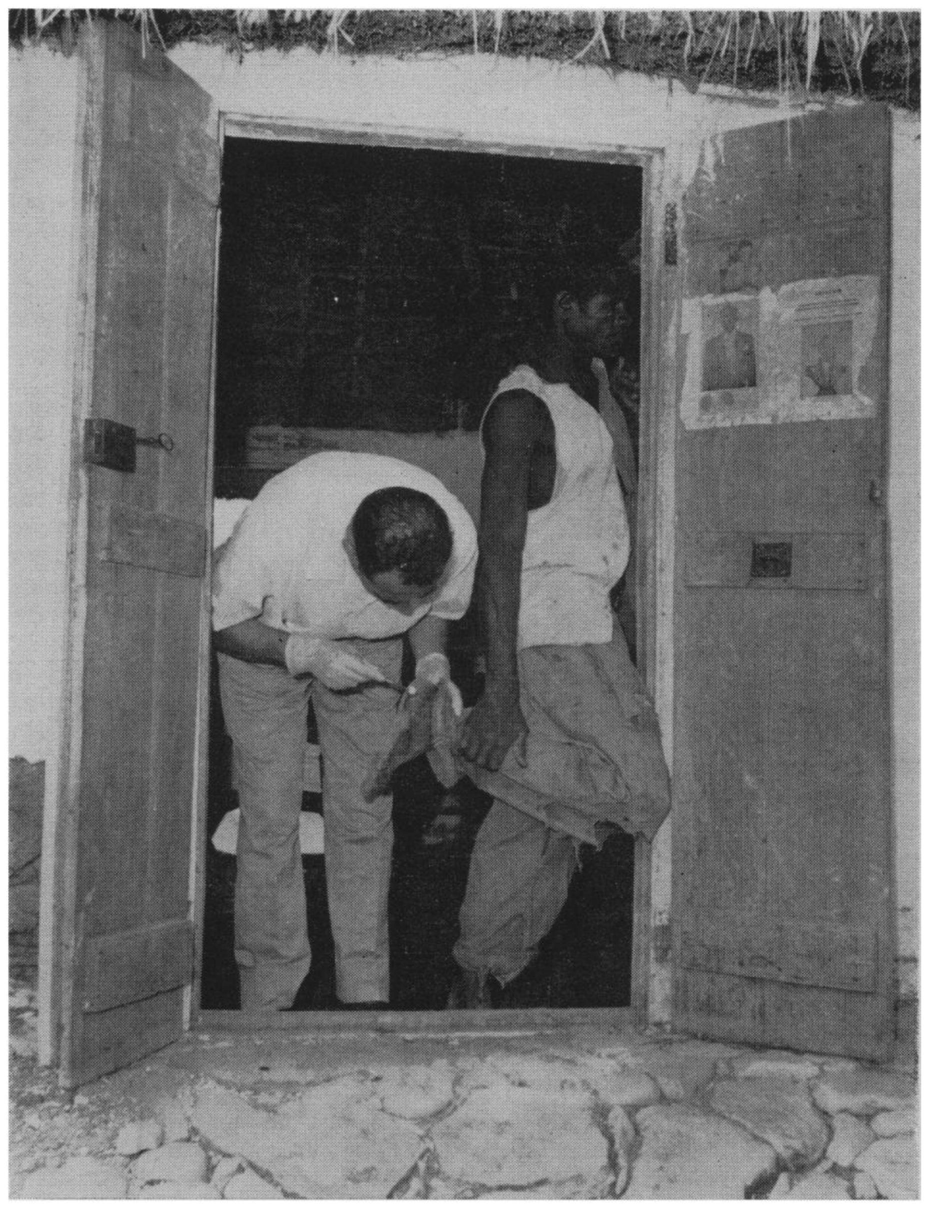

Fig. 2. "Show your feet" is the order of the day in Haiti, where, with the assistance of the Pan American Sanitary Bureau and the United Nations International Children's Emergency Fund (UNICEF), the government is carrying out a program to eradicate yaws. Signs of the infection are frequently found on the feet. UNICEF contributes equipment and supplies, while technical advisory services are provided by the Pan American Sanitary Bureau, executive body of the Pan American Health Organization and regional office of the World Health Organization. [Pan American Health Organization]

By 1871 the annual death rate per million people was down to 1012, and in the ten-year period 1911–1920, not a single death was reported. However, a very mild form was common during the 1920's (*17*). Vaccination is no longer compulsory, and the immunity status of the nation is no longer so high, so that introduced infections every few years cause small outbreaks, but smallpox still is not an endemic disease.

Glanders in England was eliminated by slaughtering all horses with the infection.

There has been almost no plague in England since the 17th century, partially as a result of the change in the species of rats in the island, and partially because of the vigorous campaigns at ports to keep out foreign rats. However, in the early 1900's, sylvatic plague was discovered in East Anglia, where a handful of human cases was diagnosed, and this persisted for a few years until it died out spontaneously. Presumably it had been introduced at a nearby port.

Higher standards of living and greater cleanliness were responsible for the disappearance of typhus and relapsing fever, for body-lice infestations are uncommon, although infestation with head lice still is found. Cholera has not been seen since the 1860's as a consequence of improvements in sewage disposal and management of water supply. Malaria has disappeared, partially because of the draining of the marshes and partially because its foothold in the country was always precarious as a result of the low summer temperatures. Also, the vector mosquitoes prefer feeding on animals to feeding on human beings.

Ceylon is another island with a good record of eradication of infections. Within the past 20 years, smallpox, plague, and cholera have all been wiped out, although each is likely to be reintroduced from time to time from India, which is only 18 miles away, across the Palk Strait. Smallpox was dealt with by maintaining high levels of vaccination immunity. Cholera and plague were both introduced infections which responded well to orthodox public health measures. The plague-carrying fleas had been imported from India and were limited to the port area of Colombo and to one or two small sites on the coast; rat-control measures have caused the infection to die out (*18*).

As for eradication on a regional scale, in America north of Mexico, several infections have disappeared. The last reported case of smallpox authenticated by isolation of the virus was in 1949 in Hidalgo County, Texas (*19*). Malaria dwindled with drainage of swamps and mosquito-proofing of homes. Control projects such as those of the Tennessee Valley Authority and the Malaria Control in War Areas were also effective, so that by the end of World War II the surprising discovery was made that, without widespread use of DDT, malaria as an indigenous infection had practically ceased to exist, although it is continually being imported (*20*).

Yellow fever was easily eradicated in the United States, once the mosquito vector had been identified, and so far it has not been reintroduced. The last cases of yellow fever were in New Orleans in 1905, when about 1000 deaths occurred (*6*). There has been no cholera for nearly 100 years.

Smallpox

Smallpox is the ideal target for an eradication program on a world scale. Since the layman, terrified by its threat, can see that it is infectious, control and eradication measures usually receive full backing, even in primitive areas. Vaccination gives a solid immunity for about three to five years and a modified immunity for life. The vaccine is easy to make on a mass scale, even under field conditions, and remains potent for seven to ten days, without refrigeration, in the "wet" form and for six months to a year in the "dry" form. Little in the way of highly skilled technical help is required, except for overall direction and evaluation, for the techniques of vaccination are simple (*21*) (Fig. 3). The chances of the infection's evolving again are small.

Malaria

Malaria has often been described as man's number one killer. The discovery of residual insecticides gave rise to the hope that at long last a way had been found to deal with the menace. The subsequent appearance of resistance to insecticides led to the belief that, if this new weapon was to be effective, it had to be used once and for all, before its edge was blunted by this resistance. The objective of world eradication has been proclaimed by the World Health Organization, supported by the United States, and agreed to by many nations, and programs are now in progress in a number of countries. No one envisioned the task as being easy, but unexpected difficulties are arising. Where transport, communications, health services, and supplies are poor or ineffective, especially in the less developed areas, the campaigns suffer.

The practical difficulties of malaria eradication are so formidable that the time for completing the program with current weapons must be measured in decades rather than in years. At least 20 years will be required and perhaps many more.

This period will be shortened drastically only if research produces new and more efficient techniques of killing insects or eliminating plasmodia on a mass scale. In any country a minimum of ten years' surveillance is necessary to insure that the last parasite has been killed. This was illustrated recently in the United States when a small pocket of infection was found in Oklahoma, several years after the indigenous infection was supposed to have disappeared (*22*). If this can happen in the United States it is even more likely to occur in countries with primitive health services.

If and when the last plasmodium parasite in a human being has been killed, and eradication on a world scale has apparently been achieved, the next question will be how to deal with similar parasites in animals, particularly monkeys and apes. Elsewhere it has been proposed that human and simian malaria are variants of the one ancestral parasite (*10*), the ape and monkey plasmodia being closely related to, or even identical to, the human parasites. Recently, natural transmission of simian malaria to human beings has been reported (*4*), and this opens up the disturbing possibility that malaria is a zoonosis, somewhat like yellow fever. Obviously this matter needs further research. If a simian reservoir does indeed exist, then eradication of malaria as presently contemplated will not be possible.

Poliomyelitis

Eradication of poliomyelitis virus is also being discussed. Production of live attenuated virus for use as an immunizing agent gives some hope that, through oral vaccination of large numbers of individuals, the wild virulent strains

Fig. 3. Lady volunteers in Khulna, East Pakistan, trained in the technique of smallpox vaccination. In countries that have the purdah system, male technicians cannot vaccinate the women, and professional women health workers are very scarce.

will be replaced by harmless strains. What is being suggested is a practical test of a bitterly fought theoretical problem, known to biologists as Gause's principle or the "competitive exclusion" principle of Hardin (*23*). In its simplest form this can be stated as follows: "Two related species of the same ecology cannot live together in the same place," for one species will have an advantage over the other and in time will replace it. The question in poliomyelitis will be, which species will survive, the virulent wild virus or the vaccine? If it is proposed merely to release doses of the vaccine in the hope that it will spread under its own agency and replace the other virus, then the effort is almost certainly doomed to failure, for the wild strains have been selected under intensely competitive conditions over long periods and presumably are far better adapted to life under natural conditions than is any "hothouse" laboratory strain that is liberated. The all-important capacity to resist adverse circumstances while being transmitted from host to host in nature has been ignored during the passage procedures in the laboratory, for passive transfer by syringe or pipet is not likely to have encouraged the selection of strains resistant to adverse conditions outside the body. As a result, the vaccine virus can be expected to have relatively little capacity to move to new hosts, as compared with the wild strains, and is unlikely to become established as a self-perpetuating organism. The experience of the Russians has shown that about 50 percent of protected persons excrete live vaccine within three to five months after vaccination (*24*), but in contrast it is well known that during epidemics of the wild strains, almost everyone in a small, intimate community is infected. Experience in the United States indicates that the vaccine virus spreads poorly and does not establish itself as a permanent infection (*25*). The differences in spread in the U.S.S.R. and in the United States may be related to variations in sanitary conditions.

Elsewhere it has been proposed that for every infection and set of circumstances there is a minimum host population that is necessary to support the infection on a permanent endemic basis (*10*). The fact that poliomyelitis infection dies out in small communities has been recognized (*26*). In a large human population, the number of individuals susceptible to the virulent poliomyelitis infection can be reduced below this threshold level by repeated feedings of the competing attenuated and immunizing live virus. When this threshold is passed, the virulent wild virus will automatically die out. The percentage of susceptible individuals in the community that form this threshold population will vary from one population to another, being lower where the chance of person-to-person contact is high, as in areas with, say, 1000 persons per square mile, and high in areas with only five or ten persons per square mile. To state this another way, it may be necessary to immunize 90 percent of the people in a town and only 75 percent in a rural area to reach the threshold level at which the wild virus disappears.

In eradication programs confined to a continent, there will be no means of keeping out reinfecting imported strains, for there is no practical way of detecting carriers of poliovirus. This means that occasional cases of poliomyelitis will occur, but that, at the worst, any epidemic resulting will be small and sharply limited. It does not follow that, if the whole world were brought up to the required level of immunity and the wild strains of virulent virus became extinct, these strains would have been eradicated for good and all further efforts could be abandoned. The circumstances that led to the evolution of the wild strains will presumably still be operative, and natural selection would quickly produce new strains from the vaccine virus, so that the immunizing procedures would have to be maintained indefinitely. By practical definition, this situation would be one of control and not eradication.

Cholera

Cholera as an endemic infection is now confined to small areas of Southeast Asia, principally the Bengal area of India and East Pakistan. Elsewhere it has been suggested that the infection is basically a rural one and is due to the fact that the only sources of water in the dry hot months are the highly polluted "tanks" or ponds of surface water (*27*). If these tanks were replaced by water supplies from unpolluted sources, then there is a good possibility that cholera would disappear from the world. Of course, Bengal is not unique in having such a situation, and similar choleraic-disease-causing vibrios might evolve in pond water in other parts of the world. Such a situation seems to occur in Indonesia, where repeated outbreaks of "paracholera," due to a different vibrio, are reported. Steps are now being taken to provide the people of Bengal with clean water; if these are successful, cholera may well disappear completely, although paracholera may persist.

Discussion

Eradication has been demonstrated many times to be entirely practical within certain limits, even with the techniques of today. Modern research is proceeding so quickly that many tasks that now seem impossible or extremely tedious and time-consuming may tomorrow be quite simple and quite rapidly performed. Most of the practical difficulties listed earlier in this article may be resolved in one or two decades.

Presumably, there will be rapid improvement in such areas as transport, logistics, and the strengthening of health services. Tasks such as the inoculation of people by the tens of millions will be speeded up by machines such as the hypospray jet injector (*28*). The dosing of people with drugs through additions to food or drink will make mass chemotherapy a practical matter. The development of live vaccines that can be given orally to babies soon after birth may immunize the populations of the world against many viruses. Such techniques, which are emerging in the laboratory today, may be available for use in the field in the near future.

Therefore, we can look forward with confidence to a considerable degree of freedom from infectious diseases at a time not too far in the future. Indeed, if the present pace of research and the present increase in the world's wealth continue, and if we suffer no major calamities such as an atomic war or an uncontrolled population explosion, then it seems reasonable to anticipate that within some measurable time, such as 100 years, all the major infections will have disappeared. This desirable goal will not be easily reached, for the difficulties are many, and unpleasant surprises are inevitable. Most of all there must be very much more research. And even as we are successfully eliminating one set of infections, new ones will almost certainly appear, for we live in a world swarming with potential pathogens in many forms. Evolution is not merely something that happened in the past; it is an essential part of both the present and the future, so that out of all the microorganisms that are continually seeking to invade our bodies, one that is favored by changing conditions will occasionally succeed. Always we will have to be on our guard, watching for signs of danger among the potential pathogens and stamping out the latest comer among them in the small focus in which it is evolving, and before it has the opportunity to spread across the world.

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