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# POXVIRUS INFECTIONS IN HUMANS FOLLOWING ABANDONMENT OF SMALLPOX VACCINATION

Smallpox vaccine
Poxvirus infections

by

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SUMMARY

The last case of smallpox in the world occurred in October 1977 in Somalia. Transmission of this disease may now have been interrupted, although we must wait another 18 months before the world can be certified smallpox-free. During this time intensive surveillance will continue in Eastern Africa and neighbouring countries and special surveillance activities will be carried out in many others. Laboratories retaining variola virus will be reduced in number and maximum containment assured.

Animal poxviruses, including monkeypox, do not appear to be a public health problem but further work is needed. Surveillance for human poxvirus disease will continue in areas of Zaire where human monkeypox cases have occurred and where whitepox virus has been found. Laboratory differentiation of whitepox virus from variola virus and further development of serologic tests for differentiating various orthopoxviruses will remain important laboratory priorities.

Abandonment of routine vaccination after smallpox is eradicated will eliminate unnecessary vaccination complications and save money. There is no evidence that epidemics of smallpox or diseases caused by other orthopoxviruses will occur once routine vaccination is stopped. Vaccinia virus will be retained indefinitely, although the use of these stocks is unlikely.

## INTRODUCTION

There have been no smallpox cases recorded anywhere in the world since the last case was found in Merka Town, Somalia, in October 1977.[1] Does this mean smallpox is indeed gone or will it reappear? Is the basic premise true that there is no animal host of variola virus? Will other poxviruses fill the ecologic niche left by smallpox, adapt to humans, and endanger the global programme?

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Considering that global eradication of smallpox is now imminent, it is appropriate to briefly review the following issues as they relate to the global programme and the post-eradication era:

(1) Reappearance of smallpox from hidden foci in human populations.

(2) Danger to humans from variola virus strains retained in laboratories.

(3) Danger of variola virus on inanimate objects and "reactivation".

(4) Current knowledge about human monkeypox.

(5) Importance of whitepox virus.

(6) Possible animal reservoirs of variola virus.

(7) Danger posed by other animal poxviruses to humans.

(8) Role of surveillance, vaccinia and vaccination.

## THE GLOBAL SMALLPOX ERADICATION PROGRAMME

One of the most sacred principles upon which the global smallpox eradication programme was conducted is that humans are the only natural hosts and vectors of variola virus. In addition, almost all individuals with smallpox develop a clinically characteristic disease. No carrier status exists. Patients are infectious only from the beginning of their illness until the last scabs fall off, a period of about four weeks, after which time they are immune to a second attack. Vaccination can provide virtually 100% protection. Thus, smallpox is amenable to eradication.

When the World Health Organization's intensified global smallpox eradication programme began in 1967, there were 33 countries with endemic smallpox (Fig. 1). The total population in these countries was over 1200 million and it is estimated that two million cases of the disease occurred that year.[2] Prior to 1967, these nations had been attempting to control or eradicate smallpox but progress had been slow.

During the programme, WHO collaborated with Member States in a variety of ways. WHO provided field epidemiologists and administrators, arranged the supply of heat stable vaccine and its national production, established quality control of vaccines, provided services for laboratory diagnosis of suspect cases, sponsored training seminars, facilitated financing and was a catalyst in a variety of other ways.

The programme has been successful. Fig. 2 shows the number of countries reporting one or more cases each year. More than seven months have elapsed since the onset of the last reported case in the world. Aggressive active surveillance persists in Somalia and neighbouring countries and will continue for another 1-1/2 years until worldwide smallpox freedom is assured.

## RISK OF SMALLPOX REAPPEARANCE FROM HIDDEN FOCI IN HUMAN POPULATIONS

The current and future risk from smallpox is related to how sure we are that transmission has been interrupted. This is proportional to how effective surveillance is in countries which have not reported cases.

When the programme first began it was found that less than 5% of smallpox cases were ever reported in many countries to national health authorities through a routine reporting system.[3,4] Thus, it was necessary to institute active surveillance, whereby smallpox cases were sought by specially trained personnel. By going from house to house, by checking facial scarring (concentrating on schoolchildren and children born since the last case was reported), by collection of specimens from persons with fever and rash, by checking health unit registers, and by using a highly publicized reward system, the efficiency of smallpox detection has been greatly improved. These aggressive approaches have been most effective during the last years of the programme. When smallpox incidence had decreased to low levels, the case detection rate approached 100%. When transmission was apparently interrupted in each country, preparations began for certification of freedom from smallpox.

To qualify for certification of smallpox-free status a country must have been free of the disease for at least two years. Smallpox history and eradication activities must be adequately documented. Countries must also provide proof of smallpox-free status by rigorous field exercises, which include the further collection of specimens from patients with fever and rash. An assessment of facial pockmarks in countries where variola major was prevalent is done to detect any cases which may have occurred since the last case was reported. In brief, the country must prove that the surveillance system is adequate to detect cases in the country if they existed.

Four countries found cases after extended periods following presumed smallpox freedom (Table 1). The range was from 6 to 34 weeks. In each instance the cases were related to prior outbreaks of human disease. Containment was rapid and further spread did not occur.[5]

Since 1973, 46 countries have been certified smallpox-free (Fig. 3). Their population is over 1100 million. Surveillance in these countries has continued; in no instance has smallpox reappeared in any country after being certified smallpox-free.

Even in the best programmes populations were never more than 80% immune, as indicated by the presence of a vaccination scar; this means there are at least 200 million unprotected people, living in areas recently endemic with smallpox. Despite this, the disease has not reappeared. In addition, the observation that smallpox freedom can persist for several decades has been borne out in Australia, New Zealand and Madagascar where chances of importation were slim due to their geographical isolation.

Another theoretical consideration regarding surveillance is related to the role of health units if smallpox transmission would persist. Experience has shown that in a given smallpox epidemic someone who is clinically ill comes to the notice of the national health service. Smallpox secondary attack rates generally have varied from 35% to 45% amongst susceptible close contacts.[6,7] If we begin with 100 index cases of smallpox in a partially immune population it will take a rather substantial number of persons to sustain the epidemic over a two-year period. For example, using a 45-50% attack rate, if each case gives rise to one case among 10 new close contacts, eight of whom are immune, then at the end of two years over 5000 cases would have occurred. It is unlikely that news of the epidemic would not reach national, neighbouring country, or international health authorities within a two-year period.

HUMAN INFECTIONS FROM LABORATORY ACCIDENTS

Currently the only known source of variola virus, and potential for future smallpox epidemics, resides in laboratories retaining such stocks. Since 1975 WHO has polled all countries and territories in the world regarding maintenance of variola virus stocks in laboratories; 180 of 181 countries and areas have responded, Democratic Kampuchea being the exception. A review of the world's literature since 1950 was also undertaken. Contact was made with diagnostic laboratories which might have worked with variola in the past. Seventy-five laboratories with variola virus were identified. Six of these were WHO Collaborating Centres for Poxvirus Research.

The Thirtieth World Health Assembly (1977) recommended that variola virus be retained only by WHO collaborating centres under conditions assuring maximum safety. Sixty-one laboratories have voluntarily destroyed or transferred their stocks; 14 laboratories currently retain variola virus (Fig. 4). The goal of WHO is to reduce this number to no more than four laboratories by 1980. Security measures for such laboratories were formulated by a group convened by WHO in 1977. The importance of strict control was shown in 1973 in London. Two persons died from smallpox after being infected by a laboratory worker, herself infected by variola virus in a laboratory.[8]

VARIOLA VIRUS ON INANIMATE OBJECTS AND "REACTIVATION"

The question of some other potential sources for future outbreaks of smallpox has recently been reviewed carefully by Dumbell.[9]

The viability of virus on inanimate objects has caused concern as it was reported in 1968 that scabs kept at room temperature on a shelf in a European laboratory for over 13 years had viable virus.[10] More recent experiments, measuring virus decay under tropical conditions, showed that infected scabs, having between $10^4$ and $10^7$ virions per gram, lost 1 log of titre every three days at 35°C and 65% humidity.[11] Considering the climate in tropical areas, it is estimated that virus concentration in scabs may decrease to a non-infective level within three weeks. Furthermore, experience during the last 11 years is that there has never been a "spontaneous" case of smallpox which could not be epidemiologically linked to other human cases or to a laboratory incident.

Variolation is the practice of inoculating material taken from skin lesions of patients with active smallpox into the skin of healthy persons to protect them from the disease. This danger has been evaluated. Samples of variolators' stocks have been collected from Afghanistan, Ethiopia and Pakistan during the last 10 years. Of 21 specimens, 17 did not grow variola virus despite the fact that several specimens showed numerous poxvirus particles in electron microscopy (Table 2). No viable virus was found nine months after scabs were collected from a patient during repeat testing. Afghanistan, where variola virus was isolated from variolator's scabs, has maintained freedom from smallpox for four years since the last case was recorded. Experience has shown that variolation ceased in the few countries where it was practised when there were no more smallpox outbreaks.

The question of variola virus remaining latent in human cadavers has been raised by Razzell.[12] He referred to a few outbreaks of smallpox occurring in eighteenth century England following graveyard contact of unsuspecting persons with exhumed cadavers. These are poorly documented events and must be viewed with the knowledge that smallpox was endemic in the United Kingdom at the time. More important is that there has been no evidence of smallpox infection caused by this mode of transmission in any countries where smallpox was rampant during the last several decades, when modern investigative methods have been used.

Other possible mechanisms which might create strains of orthopoxviruses epidemic for humans, include transformation, reactivation, or recombination. These alterations have been considered by Fenner[13] and Dumbell.[9]

Earlier views held that vaccinia virus evolved from variola through animal passage or arm to arm transfer. Thus, it was considered possible that vaccinia could be retransformed to variola virus in the way that pneumococci were noted by Griffith[14] to exchange their genetic characters. This theory was furthered by the observation in 1936 that fibroma virus could be "transformed" into myxoma virus, both being poxviruses unrelated to vaccinia. However, the mechanism was found to be "reactivation", the rescue of a heat inactivated poxvirus affected by another which is rapidly multiplying, and not "transformation".[15] In addition, Herrlich et al. have tried a number of different experimental methods to produce transformation of variola viruses into vaccinia virus and all have failed.[16] On a practical level, it appears extremely unlikely that variola virus would be reactivated in the field. Poxviruses do mutate and recombine but, as stated by Dumbell, "it is impossible to propose any parentage for a recombinant with the properties of variola, nor is there any known natural model for recombination in poxviruses".[9]

MONKEYPOX

von Magnus first reported the isolation of a simian poxvirus in 1959.[17] The strain came from an outbreak of pox-like disease amongst laboratory Cynomolgus monkeys in Copenhagen, hence the name monkeypox. To determine the real incidence of monkeypox outbreaks in captive monkeys a survey of 27 laboratories from 11 countries was conducted in 1968, and 51 laboratories from 25 countries were contacted in 1970. To 1969 there were 10 episodes where monkeypox virus was isolated from non-human primates in captivity, or from their organs.[18,19] In one instance monkeypox virus was isolated from an ant-eater which temporarily shared a cage with an infected monkey. No human infections have been associated with these outbreaks.

Monkeypox virus is an orthopoxvirus with biological properties quite distinct from variola (Table 3).[20] The virus was considered a laboratory curiosity until 1970 when the first case of human disease was discovered in Basankusu Province, Equateur Region, Zaire.[21] The case was disconcerting, as it was clinically indistinguishable from smallpox and the area had been free of smallpox for six months.

From 1970 to May 1978 33 cases of human monkeypox have been reported from West and Central Africa. Twenty-one of these have been previously summarized.[22] Twenty-five cases have occurred in Zaire, four in Liberia, two in Nigeria, and one each in the Ivory Coast and Sierra Leone (Fig. 5). Most cases, like the first, have resembled smallpox.

Twenty-six of the cases have been children nine years or less. Five persons (15%) have died, a mortality rate similar to smallpox in West and Central Africa. Four persons dying were three years or younger and one was seven. Only four patients had a vaccination scar; their ages were 35, 30, 24 and 8 years. All reported primary vaccination several years earlier, indicating the loss of immunity with time. All but one case occurred in small forest villages where people are hunters and have frequent close contact with a variety of domestic and wild animals.

Some clustering of cases has been observed, both within families and in geographic zones. The Equateur Region, one of the nine regions of Zaire, has had 14 cases from 1970 to February 1978 and the Bumba zone in the Equateur Region has reported nine cases. There were four instances where two presumed co-primary cases occurred in the same family, as there was a 0 to 3 day interval between cases. One other case lived next door to one of these family clusters and came down with the disease within 24 hours of the others. In two other families second cases occurred 9 and 12 days, respectively, after the first case; thus, secondary transmission possibly occurred, but the possibility of different exposure dates to the original infecting source other than the first case could not be excluded.

The potential for interhuman spread of monkeypox has been assessed by enumerating the number of susceptible family and community members (those without a smallpox vaccination scar) who had close face-to-face contact with patients having active disease. Of 55 susceptible contacts, only two (3.6%) came down with the disease. This secondary attack rate is quite low and it is unlikely that person-to-person transfer could continue at this rate in this environment. Tertiary spread of human monkeypox has not been reported.

Special vaccination scar and facial pockmark surveys were done in 1975 in populations living near where human monkeypox cases had occurred four to five years previously in the Ivory Coast, Liberia, Nigeria and Sierra Leone. A relatively low immunity level was found in younger age-groups. Fifty-seven per cent. of 2125 children 0-4 years, and 29% of 8047 school-age children, had no vaccination scars, indicating their probable susceptibility to monkeypox infection.[23-26] No evidence of monkeypox (or smallpox) was found in this population by house-to-house village checks or by reviews at health units in the area. This further indicates that continuing transmission of human monkeypox did not occur.

The source of human monkeypox infections is yet unknown. Epidemiologic studies have incriminated certain wild animals but only a limited number of specimens for viral culture have been taken. Earlier studies showed a low prevalence of orthopoxvirus neutralizing antibodies in mammals captured in West and Central Africa. In one survey 10 of 372 sera were positive;[27] seven were from non-human primates (four chimpanzees from Sierra Leone, two monkeys from the Ivory Coast, and one monkey from Liberia). Another serosurvey failed to detect significant antibody in over 2000 sera taken from Asian and African non-human primates, although none of these animals is known to come from areas near human monkeypox cases.[19] However, recent studies near human monkeypox cases have shown a 23% (50/215) prevalence of poxvirus neutralizing antibodies in non-human primates.[28,29]

Despite the lack of knowledge concerning the natural host and vector of monkeypox virus, recent work has shown that monkeys found near human monkeypox cases have monkeypox specific antibody.[29,30] It is only recently that serologic tests have been developed which can distinguish antibodies to the different orthopoxviruses.[30-32] These tests will serve as valuable tools during the current epidemiologic studies under way in Zaire and others which are planned.

WHITEPOX

Although attempts to isolate monkeypox virus from animals captured near human monkeypox cases have failed, four whitepox virus strains have been identified.[22] These "wild whitepox" strains came from kidney tissue of one chimpanzee, one wild monkey and two rodents captured in Zaire.[33,34] Prior to these isolations two strains of whitepox virus had been previously isolated from routine Cynomolgus kidney cell cultures in a laboratory where no poxvirus disease had been present in the institute monkey colony.[35]

The importance of whitepox virus is that laboratory tests cannot distinguish this virus from variola virus by current biological and chemical methods (Table 3).[20]

Whitepox virus can also cause a generalized rash in Cercopithecus aethiops monkeys after subcutaneous or intraperitoneal inoculation of $10^7$-$10^8$ PFU/ml (J. H. Nakano, personal communication, 1976).

However, epidemiologic evidence suggests that whitepox virus should be different from variola virus because (1) no infections with a variola-like virus have occurred in Zaire during the seven-year period since the last smallpox case was recorded, or in other areas where smallpox eradication has been achieved and (2) it can be presumed that the surveillance system is sensitive enough to detect such cases, as many monkeypox cases have been detected. Nevertheless, the finding of this virus in nature is puzzling and merits continued laboratory and field investigations.

POSSIBLE ANIMAL RESERVOIRS OF VARIOLA VIRUS

A review of smallpox occurring in wild monkeys cited several reports of "smallpox" occurring in monkey populations as long ago as 1767.[18] However, these stories appear apocryphal except for the single episode confirmed by Gispen in 1949. Orangoutangs in a Djakarta zoo, located near a smallpox outbreak, were affected by a smallpox-like infection, which possibly originated from the outbreak in Djakarta at that time. One animal died and a virus was isolated which resembled variola virus.[36]

It has been shown that variola virus can be artificially maintained in Macaca irus monkeys up to six generations, but then the transmission stopped.[37]

A poxvirus which possibly belongs to the orthopoxvirus group, but which can be distinguished from variola, was isolated from a healthy wild gerbil captured in 1968 in northern Benin (formerly Dahomey).[38] This was the only poxvirus positive isolate from among 7497 wild animals, representing at least 101 different species, captured in West Africa between 1964 and 1971.

Again, epidemiological evidence weighs against animals maintaining variola virus. No smallpox cases have been detected for several decades in areas previously heavily endemic with smallpox having large non-human primate troops which contact humans rather frequently, as in the Philippines and in Central America.

OTHER ANIMAL POXVIRUS INFECTIONS CAUSING HUMAN DISEASE

Among the orthopoxviruses (Table 4),[20] cowpox virus is pathogenic to man in addition to variola, monkeypox and vaccinia viruses. Person-to-person transmission of cowpox is, however, extremely unusual. The wide range of animal poxvirus hosts and reservoirs has been well reviewed by Baxby.[39] Many of these poxviruses such as the cowpox-like viruses (including elephantpox, carnivorepox, buffalopox), raccoonpox, camelpox, appear to be of no epidemiological importance since human infections with these agents are extremely rare or have not been well documented.

SURVEILLANCE, VACCINIA AND VACCINATION

Although the global smallpox eradication programme is concluding, poxvirus surveillance will continue, especially where human monkeypox cases and whitepox virus have been found. Special studies have already begun in Zaire to further define the epidemiology and ecology of monkeypox and other animal poxviruses.

The capability for poxvirus diagnosis will have to be maintained in the future. Research, involving the differentiation of variola and whitepox viruses, differentiation of antibodies to variola virus from antibodies to other poxviruses, and comparison of variola viruses and monkeypox viruses, still has importance and will be supported by WHO under special situations. The research and surveillance programme will be further appraised in two years when eradication will have been confirmed.

Should vaccination continue? Once worldwide eradication is certified it would be difficult to justify continued routine vaccination of all persons if there were no danger from smallpox. Complications from vaccination are infrequent but do occur, and death following post-vaccinal encephalitis occurs about once in one million primary vaccinations.[40,41]

The approach of many disease-free countries has been to develop and continually strengthen their surveillance systems to rapidly detect and contain an imported case of smallpox or other rare and dangerous tropical diseases.

Following global eradication WHO will ensure that 200-300 million doses of smallpox vaccine will be available for distribution in case of an emergency. Individual countries may also wish to maintain vaccinia seed strains and to stockpile smallpox vaccine. In all probability this vaccine will not be used.

How much will stopping vaccination predispose populations to smallpox or other poxvirus infections mentioned above? So far 16 countries (Australia, Austria, Belgium, Canada, Chile, Denmark, Finland, the Federal Republic of Germany, Japan, the Netherlands, New Zealand, Norway, Portugal, Sweden, the United Kingdom, and the United States of America) have stopped routine vaccination after carefully weighing the risks and benefits. In no instance has indigenous smallpox recurred. Although there were 52 importations of smallpox into technologically developed countries between 1951 and 1974, smallpox did not reestablish itself in any of these countries, despite the fact that the immunity levels were poor in some instances.[42,43]

It is estimated that the worldwide annual savings from stopping routine vaccination will be over 1000 million US dollars. This was spent for vaccine and vaccine administration, treating vaccine complications, time lost from work and international quarantine.

Of course, persons working with smallpox virus or other poxviruses in laboratories should be vaccinated. A few others who see and treat human monkeypox cases should be vaccinated as well.

## CONCLUSIONS

Smallpox transmission throughout the world appears to have been interrupted. To verify this observation active surveillance continues near the last known foci in the Horn of Africa and in other countries where freedom from smallpox will be certified over the next 18 months. During this time laboratories retaining variola virus will be reduced in number and maximum containment of these strains will be assured. Animal poxviruses, including monkeypox, do not appear to menace the global smallpox eradication programme but field surveillance and laboratory studies will continue.

Abandonment of routine vaccination in smallpox-free areas with low epidemiologic risk will eliminate vaccination complications and save money. There is no evidence that recrudescence of smallpox or other poxvirus infections will occur following discontinuation of smallpox vaccination. Vaccinia virus will be retained indefinitely although the use of these stocks is unlikely.

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TABLE 1

SUMMARY OF EPISODES IN WHICH SMALLPOX FOCI REMAINED UNDISCOVERED FOR LONG PERIODS

| Country | Duration of period of missed focus (weeks) | No. of cases | Date of discovery | Date of last case |
|---|---|---|---|---|
| Brazil | 15 | 18 | 2 March 1971 | 5 March 1971 |
| Botswana | | | | |
| No. 1 | 13 | 19 | 7 March 1973 | 15 April 1973 |
| No. 2 | 27 | 5 (11-15)[a] | 20 September 1973 | 14 September 1973 |
| No. 3 | 10 | 6 | 21 November 1973 | 15 November 1973 |
| Indonesia | 34[b] | 163 | 14 December 1971 | 23 January 1972 |
| Nigeria | 22 | 84 | 21 March 1970 | 10 May 1970 |

[a] Five cases detected but 6-10 additional cases are believed to have occurred.

[b] Interval between the occurrence of the last case on the main island of Java and discovery of the outbreak. Only four weeks had elapsed since the onset of the last case in Sulawesi which lies far to the north and east.

TABLE 2

SUMMARY OF INFORMATION FROM SPECIMENS OBTAINED FROM VARIOLATORS

| Country | Laboratory Results | | | | Interval from time materials taken from patients to when tested |
|---|---|---|---|---|---|
| | Tested | EM pos. | Agar gel pos. | Variola virus isolated | |
| Afghanistan | 4 | ND | ND | 4 | 4 months and 9 months[C] |
| | 5 | 4 | 4 | 0 | 6-10 years[C] |
| Ethiopia | 1 | ND | ND | 0 | Unknown |
| Pakistan | 10 | 9[A] | 7 | 0[B] | 6 months - 4 years[C] |
| | 1 | ND | ND | 0 | 1 year |
| | 21 | 13/15 | 11/15 | 4/21 | |

EM - electron microscopic examination

ND - not done

A - one specimen showed herpes-varicella virus
B - one specimen grew vaccinia virus
C - interval unknown for 2 specimens

TABLE 3

COMPARISON OF SOME ORTHOPOXVIRUSES
(from Fenner, reference 20)

| Characteristics | Variola | Whitepox (primate) | Whitepox (rodent) | Monkeypox | Vaccinia |
|---|---|---|---|---|---|
| Isolated from | man | monkey kidney | rodent kidney | man monkeys | man |
| Pocks | small white | small white | small white | small pink | large white |
| Ceiling temperature, °C | 37.5-38.5 | 38.5 | 38.5 | 39 | 41 |
| Growth in: | | | | | |
| Rabbit skin | - | - | - | + | + |
| RK13 cells | - | - | - | + | + |
| Pek cells | + | + | + | - | + |
| Pathogenicity: | | | | | |
| Mice | low | low | low | high | high |
| Chick embryo | low | low | low | high | high |
| Haemagglutination | low | low | low | high | high |
| Special antigen | Var. | Var. | Var. | Mo. | Var.+ Vac. |
| Polypeptides | Var. | Var. | Var. | Mo. | Vac.; variable |
| Host range: | | | | | |
| Man | + | unknown | unknown | + | + |
| Monkey | + | + | unknown | + | + |
| Mice | - | unknown | unknown | + | + |
| Other | - | unknown | mastomys | ant-eater | cow |

Var. = variola; Vac. = vaccinia; Mo. = monkeypox

TABLE 4

MEMBERS OF THE GENUS ORTHOPOXVIRUS
(from Fenner, reference 20)

| Virus | Host |
|---|---|
| Variola (smallpox) | man |
| Cowpox | bovines |
| Buffalopox | buffalos |
| Camelpox | camels |
| Turkmenia rodent-pox | wild rodents |
| Ectromelia | mice |
| Monkeypox | monkeys |
| 'Whitepox | monkeys, rodents |
| Vaccinia | a derivative of cowpox |

FIGURE 1

1967 - SMALLPOX CASES PER 100 000 POPULATION

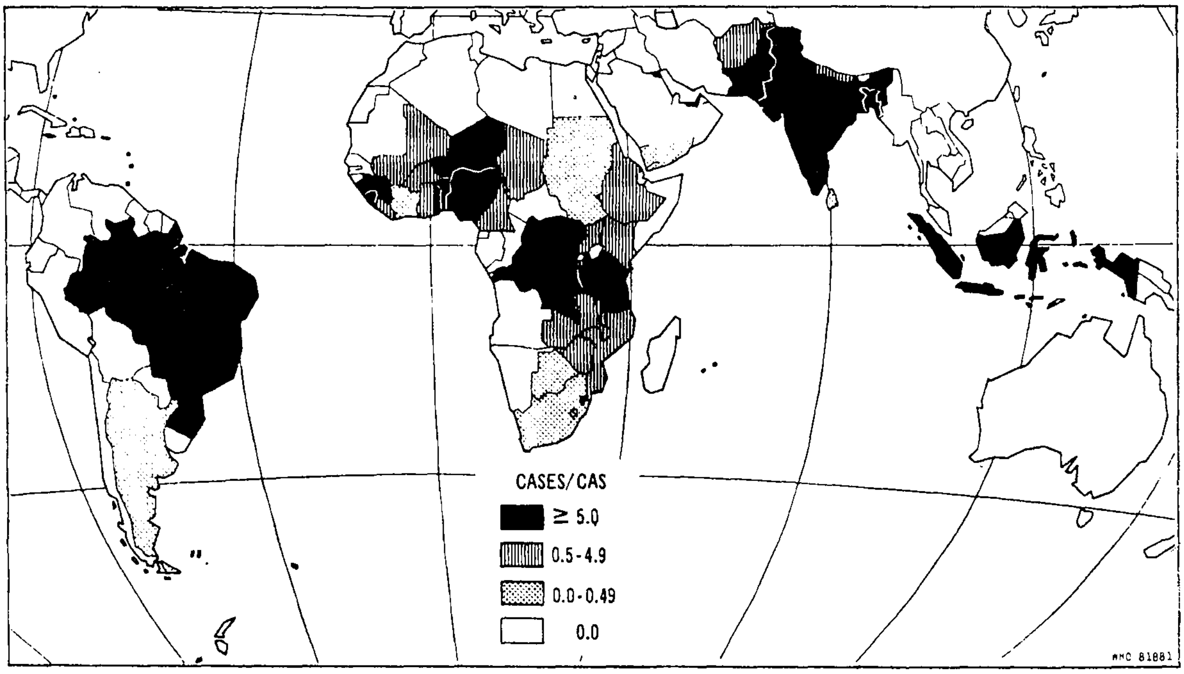


FIGURE 2

WORLD: NUMBER OF COUNTRIES REPORTING SMALLPOX BY MONTH, 1967-1978

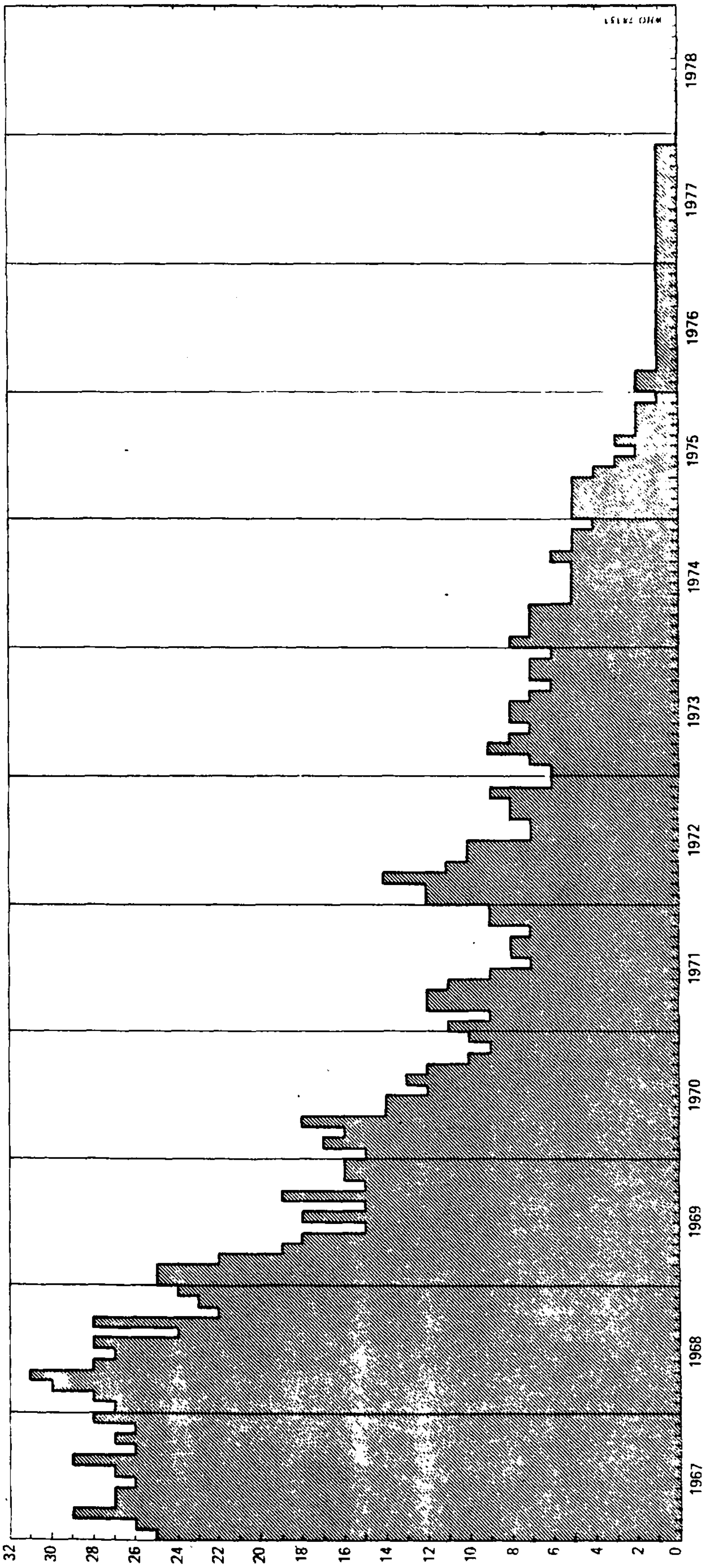
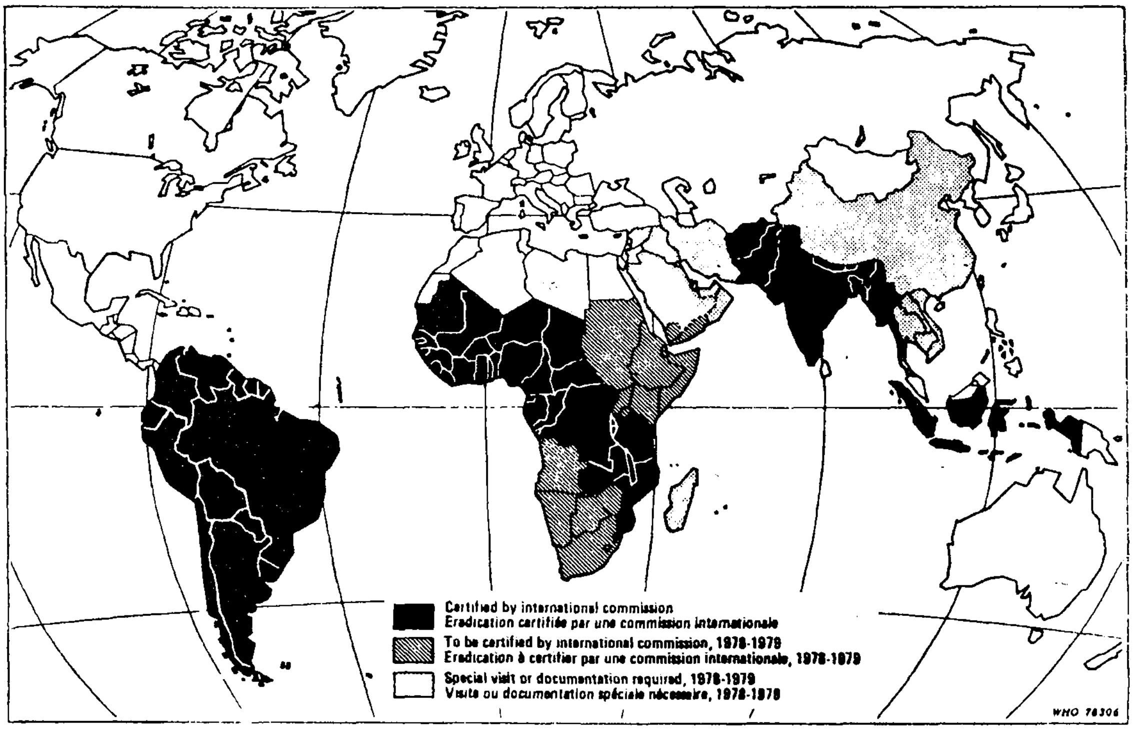


FIGURE 3

**PLAN FOR GLOBAL CERTIFICATION OF SMALLPOX ERADICATION BY THE END OF 1979**
**PLAN POUR LA CERTIFICATION MONDIALE DE L'ÉRADICATION DE LA VARIOLE D'ICI LA FIN DE 1979**




No cases of smallpox have been reported anywhere in the world for the last six months. Interruption of smallpox transmission may now have been achieved. This will be proved only after a further 18 months of intensive surveillance have elapsed without a case being detected.

Aucun cas de variole n'a été signalé dans le monde au cours des six mois écoulés. A présent, la transmission de la variole paraît être interrompue, mais cela ne pourra être confirmé qu'à l'issue d'une nouvelle période de 18 mois de surveillance intensive pendant laquelle aucun cas n'aura été dépisté.

FIGURE 4

LOCATION OF 14 LABORATORIES STILL RETAINING VARIOLA VIRUS STOCKS

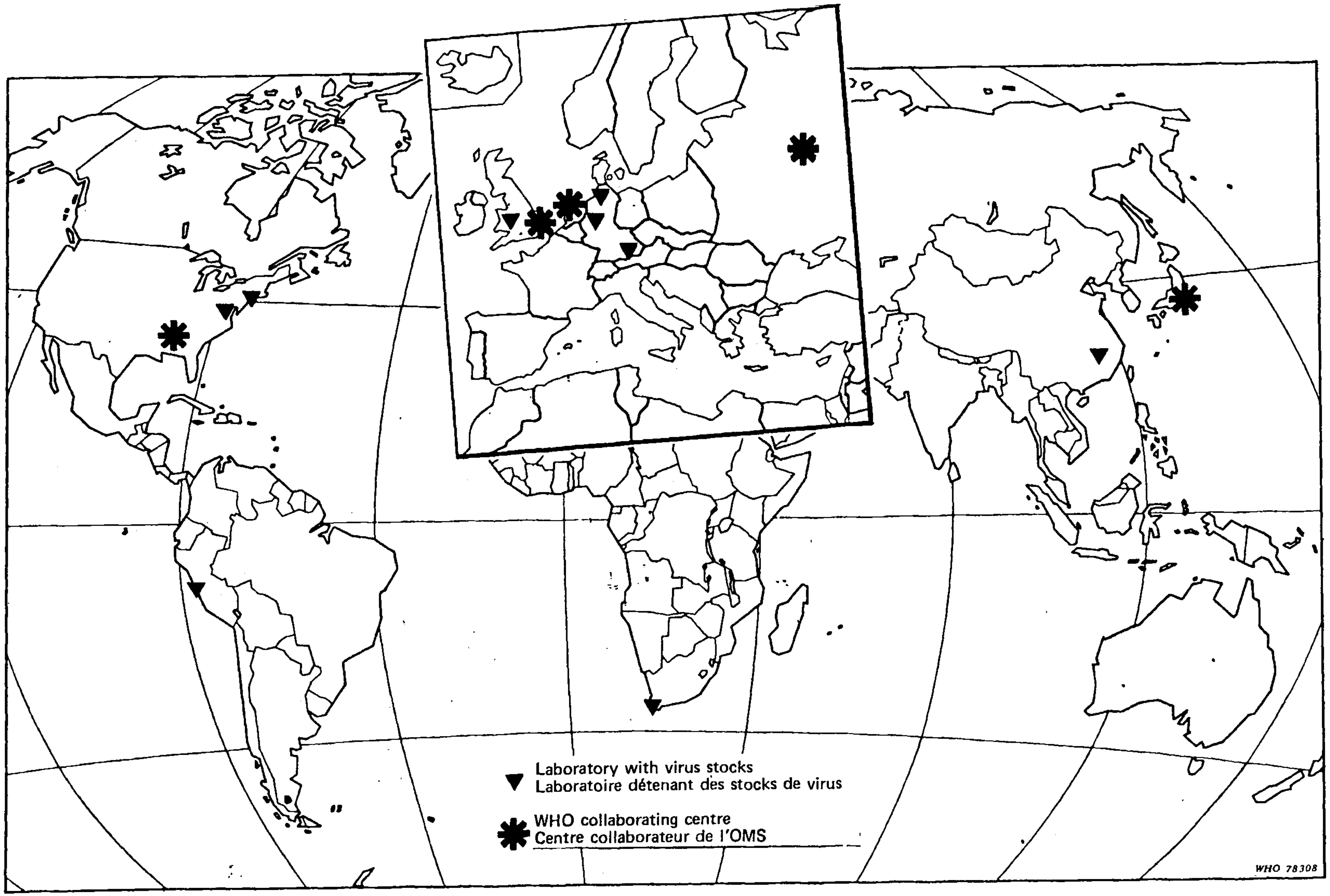
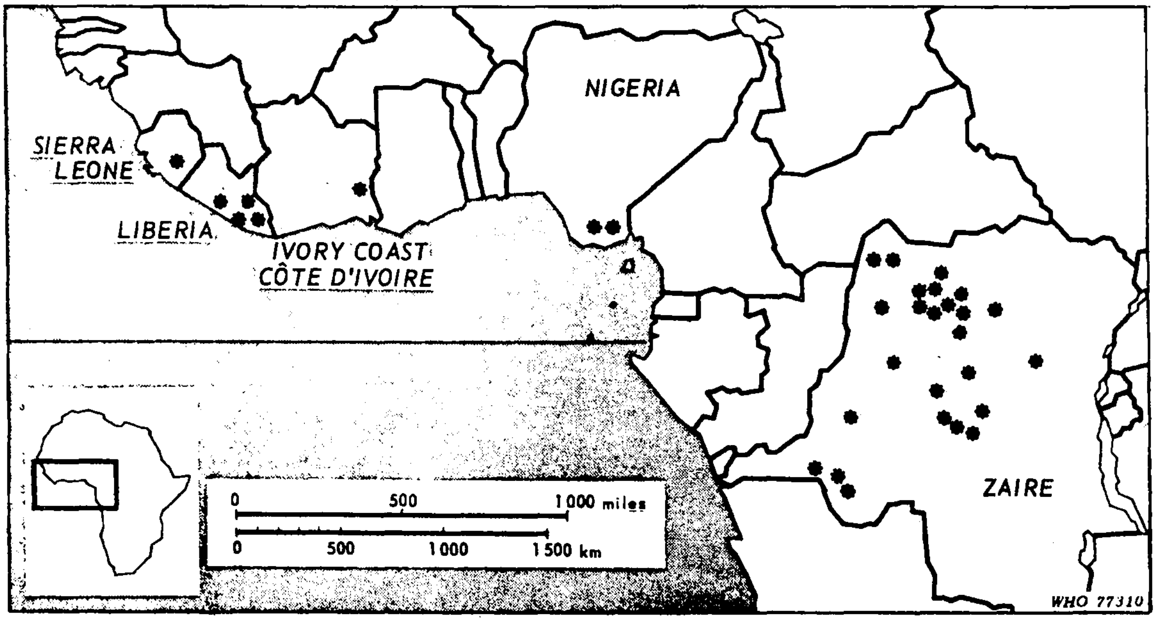


FIGURE 5

LOCATION OF 33 HUMAN MONKEYPOX CASES, 1970 - 1978 (MAY)

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