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SMALLPOX ERADICATION

(Paper for Technical Discussions)

REGIONAL COMMITTEE DOCUMENT

## Introduction

In 1958 the Eleventh World Health Assembly resolved that a concentrated effort should be made to achieve world-wide eradication of smallpox. Since then, tangible progress has been made. Countries such as Argentina, Bolivia, Cambodia, Ceylon and Thailand have succeeded in controlling the disease. In the Americas, where intensive vaccination campaigns have been in progress for several years in countries where the disease used to be **endemic**, a great reduction in cases occurred in 1963, and some of the countries have not reported further cases.

Several countries are at present developing intensive eradication campaigns which, if properly continued, promise to be successful in the relatively near future. India, the country which has reported the greatest number of cases, is making a great and powerful effort to control and eventually eliminate the disease. Unfortunately, there are still some other countries lagging behind, mainly because of inadequate health services and the lack of sufficient vaccine, equipment, transport and refrigeration. The Organization is making efforts to assist them.

In this document information will be given on the world incidence and mortality and the basic epidemiological factors of the disease. The technical and administrative aspects of an eradication campaign and the research carried out with WHO assistance will be reviewed.

An Expert Committee on Smallpox met in Geneva in January 1964. This document is mainly based on the statements, opinions and recommendations expressed by that Committee.

### 1. WORLD INCIDENCE AND MORTALITY

Since 1951 the reported number of cases in the world has dropped from about 500 000 to less than 100 000. In this connexion it should be taken into consideration that, although still defective, reporting has improved since then. With an increase in the interest in smallpox eradication and with improvement in public health services, it is to be expected that reporting will become more complete in the future.

It may then happen, as it may already have happened, that some countries will report an increasing number of cases while in fact the real number may be decreasing. It does not need to be emphasized that it is in the best interests of all countries to have as accurate reporting as possible.

Table I gives the world incidence, cases and deaths, by continents for the last five years.

Table II makes it possible to compare the number of cases and deaths notified by countries during the last five years.

In 1963, there were 92 763 cases and 24 530 deaths reported throughout the world. Of these, 75 424 cases and 22 806 deaths occurred in Asia, where India reported 60 901 and 19 436 respectively and Indonesia 7 964 and 239. Pakistan reported 5 184 and 2 868, the majority of them occurring in East Pakistan. The increase in the number of cases and deaths in India and Pakistan in relation to the previous year is due to an epidemic which affected the eastern parts of India and East Pakistan during the first half of 1963. It is interesting to note that Saudi Arabia and Thailand have not reported cases after developing intensive vaccination campaigns, and that Ceylon reported only one case in 1963.

In Africa fewer cases were notified in 1963 than in the previous two years, but this cannot be attributed to eradication efforts as these have not yet reached a sufficiently high level of development. The Congo (Leopoldville) continued to report the highest number of cases (5 496). The Congo (Brazzaville), Mali, Nigeria, Northern Rhodesia and Tanganyika each reported more than 500 cases in 1963.

In the Americas, the incidence of the disease greatly decreased in 1963, following intensive vaccination campaigns. Brazil still occupies first place, with 300 cases, followed by Columbia (144), Ecuador (45) and Peru (4).

In Europe, 4 cases were imported in 1963 and a total of 14 secondary cases and 11 deaths occurred following these importations.

The risk of importation of the disease into smallpox-free countries will continue to be present until worldwide eradication has been achieved.

TABLE I: CASES AND DEATHS BY CONTINENTS

Continent		1959	1960	1961	1962	1963*
Africa	C	13 950	15 851	24 025	24 188	16 720
	D	1 071	1 017	1 798	2 423	1 685
America	C	4 889	3 090	1 939	3 029	493
	D	-	-	-	-	28
Asia	C	58 085	39 221	53 549	46 374	75 424
	D	15 781	9 639	13 081	12 287	22 806
Europe	C	13	47	24	137	124
	D	1	-	4	27	11
TOTAL	C	76 937	58 209	79 537	73 728	92 761
	D	16 853	10 656	14 883	14 737	24 530

\*Cases and deaths notified to WHO up to 24 April 1964.

TABLE II: CASES AND DEATHS 1959-63 BY COUNTRIES

Country or territory		1959	1960	1961	1962	1963*
<u>AFRICA</u>						
Algeria	C	11	7	8	0	-
	D					
Angola	C	7		-	23	38
	D	-		-	3	1
Basutoland	C	1	-	83	52	1
	D	-	-	-	-	-
Bechuanaland	C	3	21	16	4	
	D	1	-	-	-	
Burundi	C					3
	D					-
Cameroon	C	17	-	1 345	792	133
	D	-	-	204	108	20
Central African Republic	C	-	1	-	57	3
	D	-	1	-	21	-
Chad	C	15	4	273	769	10
	D	-	-	39	150	1
Congo (Brazzaville)	C		-	22	1 254	1 515
	D		-	-	159	149
Congo (Leopoldville)	C	2 471	605	2 251	3 785	5 496
	D	64	26	149	540	706
Dahomey	C	1 708	768	119	132	228
	D	212	119	21	21	32
Ethiopia	C	352	293	761	360	232
	D	17	11	7	8	0
Gabon	C			-	1	111
	D			-	-	15
Gambia	C	3	7	12	4	52
	D	-		-	-	1
Ghana	C	99	139	70	135	23
	D	13	22	8	8	-

\*Cases and deaths notified to WHO up to 24 April 1964

TABLE II (continued)

Country or territory		1959	1960	1961	1962	1963*
<u>AFRICA</u> (continued)						
Guinea	C	439	176	-	2 948	224
	D	5	1		335	17
Ivory Coast	C	788	1 634	4 656	2 061	219
	D	35	62	237	102	10
Kenya	C	314	151	289	96	254
	D	3	5	2	-	1
Liberia	C			1 119	323	57
	D			27	10	-
Mali	C	772	1 212	1 706	1 520	1 096
	D	27	47	89	165	82
Mauritania	C	12	44	8	40	1
	D	1	-	-	-	-
Mozambique	C	1	81	51	58	85
	D	-	1	1	4	13
Niger	C	1 149	2 408	1 740	1 038	445
	D	108	127	91	107	27
Nigeria	C	1 604	4 140	3 519	3 863	1 774
	D	213	388	347	437	164
Nyasaland	C	554	795	1 465	634	455
	D	14	64	161	69	74
Portuguese Guinea	C	24	1	-	1	
	D	-	1	-	-	
Northern Rhodesia	C	47	350	233	210	1 881
	D	8	31	8	4	271
Southern Rhodesia	C	131	12	3	15	44
	D	-	-	-	-	6
Rio Muni	C		1			
	D		-			

\*Cases and deaths notified to WHO up to 24 April 1964.

TABLE II (continued)

Country or territory		1959	1960	1961	1962	1963*
<u>AFRICA</u> (continued)						
Ruanda Urundi**	C	77	19	10		
	D	-	-	-		
Senegal	C	487	6	201	231	87
	D	94	-	3	3	2
Sierra Leone	C	96	12	6	78	14
	D	-	1	1	-	-
South Africa	C		65	8	103	163
	D		±			-
Sudan	C	517	135	104	70	26
	D	86	2	-	-	-
Tanganyika	C	1 442	1 584	908	973	837
	D	158	83	45	49	47
Togo	C	64	347	281	595	274
	D	5	24	22	18	14
Uganda	C	363	707	398	628	419
	D	-	1	1	3	1
Upper Volta	C	382	126	2 360	1 335	339
	D	7		335	99	29
TOTALS	C	23 950	15 851	24 025	24 188	16 720
	D	1 071	1 017	1 798	2 423	1 685

\*Cases and deaths notified to WHO up to 24 April 1964.

\*\*Since July 1962 the independent States of Rwanda and Burundi.

TABLE II (continued)

Country or territory		1959	1960	1961	1962	1963*
<u>AMERICA</u>						
Argentina	C	34	65	6	2	-
	D					
Brazil	C	2 804	650	1 420	2 759	300
	D					28
Canada	C	-	-	-	1	-
	D					
Colombia	C	867	171	16	41	144
	D					-
Ecuador	C	1 184	2 185	496	205	45
	D					-
Peru	C	-	-	-	-	4
	D	-	-	-	-	-
Uruguay	C	-	19	1	10	
	D	-				
Venezuela	C	-	-	-	11	-
	D					
TOTALS	C	4 889	3 090	1 939	3 029	493
	D	-	-	-	-	28
<u>ASIA</u>						
Aden						
Colony	C	8	8	1	-	
	D	-	3	-	-	
Protectorate	C	62	5			
	D	24	2			
Afghanistan	C	438	111	174	303	571
	D	1	-			1
Burma	C	1 533	392	88	21	10
	D	329	53	5	-	-
Cambodia	C	4	-	1	-	
	D	-	-	-	-	

\*Cases and deaths notified to WHO up to 24 April 1964.



TABLE II (continued)

Country or territory		1959	1960	1961	1962	1963*
<u>ASIA (continued)</u>						
Ceylon	C		-	34	12	1
	D		-	8	4	-
India	C	45 115	31 052	45 204	42 478	60 901
	D	11 595	7 876	12 341	11 402	19 436
Indonesia	C	1 129	5 196	4 894		7 967
	D	478	1 000	-		239
Iran	C	288	378	123	28	6
	D	32	40			-
Korea	C	-	2	1	-	
	D	-	-	-	-	
Malaya	C	42	15			
	D	5	7			
Muscat and Oman	C	8		-	8	
	D			-		
Nepal	C			5		779
	D			2		261
Pakistan						
East	C	6 292	1 086	456	482	3 724
	D	2 737	489	197	200	2 602
West	C	1 511	912	2 518	3 030	1 460
	D	308	157	524	675	266
Saudi Arabia	C	111	32	17	1	-
	D		1			
Thailand	C	1 548	32	33	2	-
	D	272	11	4	2	-
Trucial States	C				17	-
	D				4	-
TOTALS	C	58 085	39 221	53 549	46 374	75 424
	D	15 781	9 639	13 081	12 287	22 806

\*Cases and deaths notified to WHO up to 24 April 1964.

TABLE II (continued)

Country or territory		1959	1960	1961	1962	1963*
<u>EUROPE</u>						
Belgium	C		-	1	-	-
	D					
Germany, East	C					1
	D					-
Germany, Federal Republic of	C	13	-	4	37	
	D	1	-		3	
Hungary	C					1
	D					-
Poland	C			-	32	96
	D					7
Spain	C		-	17	-	-
	D		-	3	-	
Sweden	C					25
	D					4
Switzerland	C			-	1	1
	D					-
United Kingdom	C	-	1	1	67	
	D	-	-	1	24	
Union of Soviet Socialist Republics	C	-	46	1	-	-
	D					
TOTALS	C	13	47	24	137	124
	D	1	-	4	27	11

\*Cases and deaths notified to WHO up to 24 April 1964.

## 2. EPIDEMIOLOGICAL FACTORS

Smallpox is transmitted from man to man. As no long-term human carriers exist, the infective virus is ultimately derived from the acute case. Lesions of the skin and mucous membranes contain virus in large amounts, but the most important source of virus from the epidemiological point of view is the respiratory tract. The patient should be considered as infectious from the onset of fever and is usually most infectious around the third day, when the rash appears. Consequently the most likely source of infection is contact with a patient in the pre-eruptive and early eruptive stages of the disease. Virus from the respiratory tract may be present on the skin, clothing and bedding long before the maturation of the vesicles and scabs.

Scabs have traditionally been regarded as an important source of infection, and it has been proved that the virus can remain alive in them for long periods, but in practice they do not appear to be as important in the dissemination of the disease as direct droplet transmission or droplet dust from clothing and bedding. Patients, however, should be isolated until the scabs are shed. Subsequent desquamation of the skin is not infectious.

Clothing and bedding may give rise to infections in those persons handling them. Flies which have been in contact with the skin and secretions of patients can carry the virus mechanically. As the virus remains alive in the body after death, the corpse as well as the clothing in contact with it may be infectious.

The possibility of the spread of variola virus from hospitals by air for long distances has been a subject of considerable discussion. Theoretically the virus can be carried by currents of air for a distance of 500 metres or more, but this mechanism of transmission has never been definitely proved to have caused the outbreaks which sometimes have occurred in the proximity of smallpox hospitals. The infection by missed cases, the possibility of accidental contacts with patients in the pre-eruptive stage of the disease, or the coming into contact with imperfectly disinfected clothes can never be completely ruled out.

The early case, and not the convalescent case with many scabs, is the most probable source of infection. Severe and moderate severe cases seem to be more infectious, but they do not usually remain ambulant. The fulminating types seem to be less infectious and the abortive cases may be infectious only for a short time - sometimes a few hours.

Early isolation is very important because, if the patient is kept at home, the other members of the family are exposed to a great risk. The larger the household and the greater number of young susceptible adults in a community, the greater the chance of the spread of the disease. Ambulant mild cases may occur, especially among adolescents, and fairly severe but ambulant cases among tramps and

other itinerants. Persons engaged in the transport industry, having missed mild attacks, may carry the infection from one place to another. Doctors, nurses and other members of hospital staff, undertakers and health inspectors are especially at risk and may also disseminate the disease. It is consequently very important that they be well immunized.

Climatic factors such as temperature, humidity, etc., may account for some of the variations in incidence observed in endemic areas.

#### 2.1. Immunity after vaccination

A successful primary vaccination produces nearly complete immunity for three years in the great majority of individuals. Later it wanes gradually, and it has been suggested that the chance of acquiring the disease (variola major) if exposed to contact is reduced to  $1/8$  within 10 years,  $1/2$  within 20 years and relatively little if any protection is afforded after 20 years. Immunity following a successful primary vaccination is more effective and of longer duration against variola minor.

It is difficult to obtain accurate information about immunity following revaccination, mainly because of the problem of interpreting equivocal reactions. However, the freedom from the disease enjoyed by medical and nursing personnel revaccinated regularly and exposed to risk of infection indicates that the regular revaccination induces a great degree of immunity.

#### 2.2 Immunity in relation to the number of insertions

There is some evidence that when smallpox occurs many years after primary vaccination not followed by revaccination, the fatality rate decreases as the number of vaccination scars increases. However, the trauma of multiple insertions and the fear of severe reactions induced by them may so increase the avoidance of vaccination that the possible improvement of immunity gained by the individual may be more than offset by the smaller proportion of the population protected.

### 3. TECHNICAL AND ADMINISTRATIVE ASPECTS OF AN ERADICATION CAMPAIGN

Regarding the possibility of eradicating smallpox, the WHO Expert Committee on Smallpox, which met in Geneva from 14 to 20 January 1964, stated:

"The global eradication of smallpox is well within the bounds of possibility. The only reservoir is man; infection is manifest; carriers do not exist, and successful Jennerian vaccination provides effective immunity. Its eradication is a matter of concern to all countries, as those now free constantly run the risk of the introduction of the infection from endemic areas."

#### 3.1 The vaccine

A very important element in ensuring the success of a vaccination campaign is the use of potent vaccines able to stand the climatic conditions of the country. Liquid vaccines are not suitable for mass campaigns in hot climates. Minor upsets in the rigid requirements for the storage and transport of the vaccine are liable to reduce the potency. This reduction may not be sufficient to lead to a fall in the proportion of successful primary vaccinations, but is often sufficient to cause a marked fall in the proportion of successful revaccinations. When this happens, the high "take" rate in primary vaccinations can be very misleading and may vitiate a campaign. Freeze-dried vaccine, which is more stable, obviates the difficulties associated with transport and storage. In eradication programmes, therefore, high priority must be given to providing adequate quantities of potent freeze-dried vaccine and to ensuring that they are handled with the precautions necessary to maintain the optimum potency up to the moment when the vaccine is applied. It should not be forgotten, however, that after reconstitution, freeze-dried vaccine becomes as labile as liquid vaccine.

#### 3.2 Administration and allocation of responsibility

Campaigns are to be conducted under the responsibility of the national government, with the technical advice and material assistance of WHO and other international organizations if necessary. Administrative and financial matters and the technical organization of the campaign are the responsibility of the national government. For the direction of the campaign a full-time senior medical officer should be appointed who should be directly responsible to the Central Health Administration. He should be well-experienced in the field of smallpox control, as well as in administrative matters. He should be able to seek help and advice from the health authorities or advisory groups and WHO officers, but he himself should take final decisions. He should be in direct contact with the Minister of Health or with the Chief of Public Health Services.

An efficient administrative organization should be established, with adequate funds. It should be responsible for the supply of vaccine and other equipment, transport, statistics and maps, health education, training and staff welfare. The smallpox eradication service should preferably be integrated into the existing structure of the public health service and its activities co-ordinated with those of other departments. In some countries where the health services are still in a stage of development, the eradication campaign has to be set up as an independent campaign. Whether integrated or independent, it should be directed centrally by the responsible officer, and at provincial or district levels an officer, preferably a medical officer, should be in charge.

If legislation for compulsory vaccination and revaccination, for notification of cases, isolation of cases and surveillance of contacts, or for quarantine measures and health education is found to be necessary, it should be prepared and measures taken for its implementation.

The campaign should be organized in three definite phases: the preparatory phase, attack phase and control or maintenance phase.

### 3.3 The preparatory phase

In this phase the epidemiological assessment of the smallpox situation in the country, as well as the recruitment of personnel and its training should be carried out. All available information about smallpox should be gathered, e.g., the number of cases and deaths which have occurred in the previous ten years; the incidence and case mortality rates; the geographic and age distribution of cases; previous vaccination campaigns and their results; the socio-economic conditions and the level of health education of the population, etc.

The actual and potential availability of personnel should be considered. The training of personnel should be done before the campaign starts and maintained during the campaign. The welfare of the staff should be taken into consideration. When eradication is achieved, the personnel released should be transferred to other public health activities where the public health experience gained during the campaign will be of value. Facilities for transportation and refrigeration must be ascertained. Arrangements should be made for an adequate supply of potent vaccine and for its storage and distribution. A programme of health education should be prepared. Decisions should be taken on the vaccination technique to be used during the campaign. Because vaccines of high potency are now available, the use of instruments which cause considerable trauma and severe reactions should be abandoned in favour of the multiple pressure or the single short scratch (6 mm) as soon as this can be conveniently arranged. The choice between these two methods will depend on local preferences.

In some countries it may be wise to organize at this stage limited pilot projects to uncover possible difficulties and to devise means of overcoming them.

### 3.4 The attack phase

This is the main part of the campaign, and its success depends largely on the measures taken during the previous phase. The time to be taken in completing this phase will vary according to the many variables, such as the size of population and its distribution in urban and rural areas, personnel available, transport facilities, terrain, climatic conditions, etc. However, it is important that the attack phase be completed in the shortest possible time: in any event it should not last more than three years.

It is imperative to begin by concentrating efforts on areas with high densities of population, whether they be urban, rural or mixed, where the disease persists and from which spread to other areas is likely to occur. When these densely populated areas are solidly protected, the maximum effort should be transferred to the contiguous areas. This is particularly the case when vaccine supplies are limited and have to be used to the best possible advantage.

The target must be to cover 100% of the population. Special attention should be paid to age groups in which the disease most frequently occurs, as shown by analysis of age-specific attack rates and to new-born children and pregnant women in whom mortality is very high. If possible, each vaccination and revaccination should be examined after 6-8 days and those persons who do not show a major reaction vaccinated again immediately. If it is not possible or practical to see the results of the vaccination in all persons vaccinated, at least 20% should be examined to estimate the success of the campaign.

The vaccinators should be organized by teams headed by an inspector, who has to supervise their work constantly and strictly. Each team should consist of 6-10 vaccinators. A medical officer should be responsible for a group of 6-8 teams. Adequate transport is essential in an eradication campaign. The requirements will depend on the nature of the terrain and communication facilities.

In countries with large populations it may be necessary to repeat this phase a second time, to carry out well planned and carefully executed mopping-up operations in order to ensure the coverage of newly arrived members of the population as well as of pockets of population that may not have been vaccinated during the first sweep.

### 3.5 The maintenance phase

As soon as one of the high density areas has been successfully vaccinated as planned, the maintenance phase should begin. Depending on the circumstances, it may be under the control of the normal public health services or combined with other special control programmes such as malaria eradication or yaws control. The vaccination of new-born

children, immigrants and floating populations and the routine re-vaccination of the whole population will be the principal activities of this phase.

An epidemiological investigation should be made of each outbreak or sporadic case which occurs and the information centralized. The spread of the disease should be controlled by vaccination of the foci of infection and other control measures. Every suspicious case should be carefully examined, and laboratory diagnosis should be made every time that there is any doubt about the diagnosis.

### 3.6 Evaluation

The success of the campaign will be indicated by the disappearance of the disease. The percentage of each section of the population vaccinated in each area will give an indication of the adequacy of the coverage. Teams must therefore keep a constant check on the efficiency of their work and on the potency of the vaccine in the field, which may differ from the potency at the time of production because of deterioration during storage and transportation. A check should be made by observing and recording vaccination reactions in representative samples of persons primarily vaccinated and revaccinated by each vaccinator.

Information on the population in the area in which the team is working, the percentage vaccinated by age groups (and if necessary by other groups such as occupation groups), the numbers of vaccinations and revaccinations which are read and the numbers successful, should be collected weekly by the team and reviewed by a responsible medical officer. This information should be transmitted weekly to the campaign headquarters for consolidation and analysis.

At the same time, an independent evaluation should be carried out by a separate team responsible directly to campaign headquarters, so that the efficiency of the work coverage will be independently checked. The level of immunity of the population after the vaccination campaign should be checked by the independent evaluation team by means of carrying out challenge vaccinations in a representative sample of the population.



4. EPIDEMIOLOGICAL AND LABORATORY STUDIES ON SMALLPOX,  
DEVELOPED WITH THE ASSISTANCE OF WHO

4.1 A better vaccine

One of the great difficulties in vaccination campaigns, especially those carried out in tropical areas, has been the rapid deterioration of glycerinated lymph vaccine. In order to solve this problem, WHO organized studies of methods to ensure the regular production of a suitable heat-resistant dry vaccine. Laboratory tests of vaccines produced by several methods in different laboratories were carried out in a comparative study in which laboratories from several countries participated. These tests showed that vaccine production based on desiccation from the frozen state (lyophilization) gave 100% successful primary vaccination rates after periods of storage up to 64 weeks at 37°C - 45°C, whereas other vaccines were less satisfactory. Information about this method of production and about subsequent technical improvements has been distributed to competent production laboratories, and assistance has been given to some of them in producing this type of vaccine. Recent studies have shown that only vaccines of the highest potency will give satisfactory "take" rates in revaccination. These findings are of obvious importance in relation to eradication campaigns. A vaccine producing a high percentage of "takes" in primary vaccinations but failing partially or completely in revaccinations not only dooms the campaign to failure but also gives a false sense of security.

4.2 The use of jet injectors

The successful utilization of jet injectors for the rapid vaccination of large numbers of persons has been reported. The Organization is in close contact with a group of investigators making well-planned extensive trials on the results obtained by the use of jet injectors in comparison with traditional methods of vaccine inoculation. Trials using jet injectors manually loaded are also being organized by WHO. If the use of jet injectors proves to be practical, steps will be taken to employ them in mass campaigns.

4.3 Passive protection

The vaccination of contacts is not always successful as a protective measure against smallpox. The chance of failure increases as the interval between exposure and vaccination lengthens. Studies have been carried out on the use of vaccinia hyper-immune gamma globulin in the prophylaxis of smallpox in contacts. These studies showed the efficacy of gamma globulin as a preventive agent.

4.4 Studies on the infectiousness of smallpox in the early  
stages of the disease and on dissemination of the virus  
by air

Epidemiological observations suggest that smallpox is not highly infectious in the pre-eruptive period of illness. The clarification of this point is of great practical importance in determining the period during which a patient may be infectious and for purposes of

isolation of contacts. Studies of this problem have been carried out with the support of WHO. No virus could be recovered from mouth washings and garglings from patients in the first two days of the disease. It was, however, frequently found in specimens collected during the 6-9 days of illness. This is further proof that most smallpox patients are not infective in the first days of fever, before the rash appears.

Experiments have been carried out to determine the amount of virus disseminated in the area of a smallpox ward and in the immediate surroundings of smallpox patients at various stages of the disease. Contrary to what was suspected, the virus was difficult to recover even when large volumes of air were collected in the proximity of acutely ill patients, though it could be isolated from the bed clothes. The infectious unit in smallpox appears to be a relatively large droplet or particle which rapidly sediments near the patient, particularly on his pillow, and is resuspended in dust particles.

#### 4.5 Chemoprophylaxis

Chemical compounds have recently been reported to have an anti-viral effect against variola, vaccinia and other viruses. One of these compounds, N-methyl-isatin-B-thiosemicarbazone, which has been shown to have low toxicity for animals and man and a high level of activity against vaccinia and variola viruses in the laboratory, has been tested in prophylactic trials against smallpox. This drug proved to be very effective even when given more than six days after contact. Further trials with different dosage schedules are in progress. Other compounds are also being studied. The discovery of the value of chemoprophylactic substances is important because although the use of these compounds does not lessen the need for routine vaccination, they may be useful in supplementing the protection afforded to contacts by vaccination after exposure to infection.

#### 4.6 Studies on variations in strains of variola virus from different areas in Africa

Variola major and variola minor both occur in Africa. There is evidence of the presence of strains of intermediate virulence, as determined by laboratory tests, in certain areas of Africa. Studies to relate laboratory findings to clinical and epidemiological findings are being set up.

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DEFINITIONS

Variola major: Typical smallpox with a case fatality rate in the unvaccinated ranging from about 20% to about 50% depending on the age distribution of the patients and on other environmental and host factors.

Variola minor: Mild form of smallpox with a case fatality rate in the unvaccinated of less than 5%. (Synonym: alastrim)

Vaccination: The cutaneous inoculation of smallpox vaccine into a person not previously successfully vaccinated. (Synonym: primary vaccination)

Revaccination: The cutaneous inoculation of smallpox vaccine into a person who has a vaccination scar or convincing documentary evidence of previous successful vaccination or revaccination.

Repeat vaccination or repeat revaccination: Reinoculation of smallpox vaccine into a person in whom vaccination or revaccination did not produce a major reaction.

Successful vaccination or revaccination: Occurrence of a major reaction following vaccination or revaccination. (Synonym: take).

Major reaction: (1) Presence of a typical Jennerian vesicle on examination one week after primary vaccination.

(2) Presence of a vesicular or pustular lesion or an area of definite palpable induration or congestion surrounding a central lesion, which may be a scab or ulcer, on examination six to eight days after revaccination.

Equivocal reaction: Any response to vaccination or revaccination other than a major reaction.