



MANAGEMENT OF SUSPECTED CASES OF SMALLPOX IN THE POST-ERADICATION PERIOD<sup>1</sup>

Contents

	<u>Page</u>
1. Introduction . . . . .	2
2. Analysis of Reports or Rumours of Suspected Smallpox notified to WHO . . .	2
3. Role of WHO . . . . .	3
4. Role of National Health Authorities . . . . .	3
5. Investigation of Suspected Cases . . . . .	4
5.1 Examination of the suspected smallpox patient . . . . .	4
5.2 Epidemiological investigation . . . . .	4
5.3 Collection of specimens for laboratory diagnosis . . . . .	5
6. Isolation, Disinfection and Observation of Contacts . . . . .	5
7. Vaccination Policy . . . . .	5
8. Monkeypox . . . . .	5
9. Relations with News Media . . . . .	6

Annexes

1. Clinical diagnosis of smallpox . . . . .	7
2. Epidemiological investigation . . . . .	9
3. Collection and dispatch of specimens for laboratory diagnosis . . . . .	10
4. Monkeypox . . . . .	12

Figures

1. Equipment for collection and dispatch of specimens from suspected smallpox patients . . . . .	13
2. Smallpox recognition card (enclosed as insert)	

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## 1. Introduction

The WHO smallpox eradication programme reached its goal when the last case of endemic smallpox occurred in October 1977. Continuing surveillance failed to discover any smallpox case and in May 1980 the World Health Assembly declared that global eradication of smallpox had been achieved. Nevertheless, many rumours of suspected cases of smallpox have been received by national health authorities and by WHO. These have been investigated, with uniformly negative results. It is evident that rumours and reports of suspected smallpox will continue to be received in the future.

It is important that these rumours, as in the past, be investigated promptly by experienced investigators and that, if they are proved to be unfounded, the public be informed that they are false alarms. Appropriate investigations can be carried out within the framework of existing national epidemiologic services and, if required, WHO will collaborate in the investigation. Only by continuing surveillance will the world remain confident that smallpox has been eradicated, thus permitting the cessation of smallpox vaccination and the discontinuation of international requirements for vaccination certificates for smallpox.

During the surveillance period, WHO was often asked whether a document on how to handle suspected cases of smallpox was available. Because there were still many health officers who had acquired a great deal of experience during the smallpox eradication campaign it was believed at that time that such a document was unnecessary. However, more than three years have now passed since the last case of endemic smallpox and these health officers have other responsibilities and may no longer be available to investigate suspected smallpox cases. Their availability will further decrease as time goes on.

This document has been prepared in order to provide guidelines for management, particularly for national epidemiologists who will encounter suspected cases of smallpox and will have to make appropriate decisions. The document is subject to modification as experience is gained through its utilization.

## 2. Analysis of Reports or Rumours of Suspected Smallpox notified to WHO

From January 1978 to December 1980, WHO Headquarters in Geneva and the six regional offices of WHO received 142 reports or rumours of suspected smallpox from national or regional health offices or from the public. Analysis of these rumours indicates that national epidemiologists are likely to encounter the following categories of rumour in the future.

### Group A: Reports from medical and laboratory facilities

(1) Errors may be made in laboratory diagnosis, such as the erroneous interpretation by inexperienced observers of non-specific material on electron-microscopic slides or the mistaken identification of pocks on chick embryo membrane.

(2) Errors in clinical diagnosis.

(3) Patients seen in hospitals or clinics with facial pockmarks may have the dating of their illness erroneously made and be considered recent smallpox victims, whereas, in fact, their illness occurred many years before.

(4) There has been one episode of laboratory-associated smallpox during the surveillance period of 1978, which was immediately contained with only a single secondary case. The very few laboratories now continuing research with variola carry on their work under maximum security conditions and the possibility of this occurring again is very remote.

Group B: Reports in publications

Errors may be made in the recording of smallpox cases in statistical reports of communicable diseases or in special press reports.

Group C: Reports from the public

- (1) Members of the public seeing chickenpox, measles, or death caused by measles, or a variety of skin diseases, may believe that the patients suffered from smallpox and submit a report to the health authorities or to WHO.
- (2) Travellers may return with vague rumours of smallpox outbreaks, usually in remote villages, refugee camps or in border areas, sometimes with many deaths. Such rumours may come from areas where variolation was formerly practised.

Group D: Monkeypox

In the tropical rainforests of central and west Africa, rare cases of human monkeypox occur which resemble smallpox and can only be differentiated from smallpox by laboratory diagnosis. These have not been reported from other parts of the world.

3. Role of WHO

WHO Headquarters in Geneva maintains a programme for post-smallpox eradication surveillance to coordinate appropriate investigation with regional offices and the countries concerned. If such reports as described in section 2 reach WHO, the staff in collaboration with regional and national personnel:

- (1) contact the informant to obtain all possible details of the incident, including patient's name, age, vaccination history, address, date of rash onset and history of contact with other smallpox-like disease;
- (2) report the rumour to the national health authority for investigation;
- (3) arrange laboratory diagnosis of specimens and expedite testing by WHO collaborating laboratories;
- (4) consult national health authorities and, if required, recruit experienced epidemiologists who participated in the smallpox eradication programme;
- (5) inform the scientific community or the public (as appropriate) of the results of the investigation.

4. Role of National Health Authorities

The national health authority should understand that if a smallpox rumour is reported within its territory, an appropriate investigation and report to the public or the scientific community is the only practical method of clarifying the rumour. Even though these rumours appear questionable they should be investigated by visits of experienced personnel to the named areas and by extensive questioning of the population, however time-consuming and wasteful this may be, in order to maintain confidence at national and international levels. The frequency of such reports will decrease when the fact of eradication is increasingly accepted.

In hospitals, dispensaries and health stations, patients will continue to be seen with rashes due to chickenpox, measles and other rash diseases and these will, on occasions, raise a suspicion of smallpox. Most questionable cases can be resolved by experienced health personnel at the local level by clinical examination. If doubt remains, however, specimens should be collected, national health authorities should be notified and the patient should be isolated. Specimens should be dispatched through national health authorities to WHO collaborating laboratories. The national epidemiologist should advise on epidemiological investigation and other measures which should be carried out while waiting for laboratory results. The national health authorities should report immediately to WHO.

## 5. Investigation of Suspected Cases

Investigation of suspected cases follows three steps: (1) clinical examination of the patient; (2) epidemiological investigation of possible sources of infection and the presence of similar illness in the area; and (3) collection and dispatch of specimens.

### 5.1 Clinical examination of the suspected smallpox patient (Annex 1)

More than 90% of smallpox cases have a typical illness which is readily recognized by an experienced observer. Important points in differentiating smallpox from other diseases with rash are the following.

(a) A vaccination scar should be looked for. Smallpox is very unlikely to occur in a person vaccinated within the prior five years.

(b) The patient becomes ill with fever, malaise, backache and headache before the appearance of the rash. This pre-eruptive phase usually lasts for two or three days. The patient becomes infectious during the last day or two of the pre-eruptive phase and remains infectious until the last scabs have fallen off.

(c) The rash begins with macular lesions which progress day by day to papules, vesicles, pustules, and scabs (crusts). At any one time the lesions on each part of the body are in the same stage of development. This is in contrast to chickenpox, in which lesions in all stages of development are seen at the same time. The rash tends to be heavier on the extremities than on the body and the palms and soles usually have lesions. This also is in contrast to chickenpox, in which the rash is heavier on the trunk than on the extremities.

(d) In the haemorrhagic form of the disease, which is very rare, the patient may die without developing a typical skin rash. In this form the patient may show areas of bleeding into the skin and conjunctivae and bleeding from the nose, alimentary, urinary and genital tracts. Hence the diagnosis may be confused with many diseases which cause generalized bleeding such as haemorrhagic fevers, meningococcal infections and others. Diagnosis is possible only by laboratory examination of the disease in the person who was the source of infection or in those whom the patient has infected.

(e) It is very useful to have a photograph of the patient's rash in case the clinical diagnosis needs to be referred to another investigator who does not have the opportunity of seeing the case.

### 5.2 Epidemiological investigation (Annex 2)

Since man is the sole host of smallpox, the disease can be maintained only by man-to-man transmission. For the epidemiological investigation the most important question is to determine how the person might have been infected. The incubation period is between 7 and 17 days, therefore at some time during this interval the patient should have been in face-to-face contact with a person with a similar illness. Information should also be sought on whether a similar disease has been occurring in the community. Information must be obtained from family, friends and neighbours. The findings will provide the basis for deciding what, if any, further investigations are necessary.

### 5.3 Collection of specimens for laboratory diagnosis (Annex 3)

If the diagnosis is in doubt, specimens of fluid from lesions or scabs must be collected for electron microscopic examination and virus isolation. If the patient has already recovered, a serum specimen should be collected for antibody testing, since it may be possible to confirm or exclude the diagnosis of smallpox or monkeypox. All the specimens should be sent to WHO, Geneva, which will forward them to one of two WHO diagnostic centres: Centers for Disease Control, Atlanta, USA, or Research Institute of Virus Preparations, Moscow, USSR. In the case of specimens collected in the region of the Americas, these may be sent to the WHO Regional Office in Washington which will forward them to the Centers for Disease Control.

National diagnostic laboratories may have the facilities to test these specimens. However, experience has shown that the reliability of test results is reduced by lack of practice and may be expected to be reduced further with time. The two WHO laboratories will maintain their competence by frequent monitoring of testing methods.

### 6. Isolation, Disinfection and Observation of Contacts

Isolation and disinfection are not necessary unless smallpox is strongly suspected by an experienced observer who has had extensive experience in the clinical diagnosis of smallpox. If the patient is isolated, this can be done at home in a village or in the isolation unit of a hospital. Only immunized persons who have vaccination scars or facial pockmarks which have been caused by smallpox should take care of the patient. The patient should remain in isolation until the laboratory report is received. Contaminated articles and the premises, if the patient dies, should be disinfected.

If the suspected case is put in isolation, any contacts should be kept under observation in their homes. They should be visited daily by an experienced observer who should give them a thorough examination for signs of rash and take their temperatures. If they have two consecutive readings of 38°C or above, they should be placed in separate isolation as suspected cases. Observation could be discontinued if contacts develop typical chickenpox or other disease which is clearly not smallpox, or if a negative report is received of the specimen submitted from the original suspected case. However, as long as smallpox remains a possible diagnosis, daily observations should be continued up to 18 days from the last day of contact with the index case.

### 7. Vaccination Policy

The past policy of immediate widespread vaccination when a suspected case of smallpox was detected is no longer justified. Vaccination should not be done unless a presumptive diagnosis of smallpox is established based on examination by a physician with extensive experience in the clinical diagnosis of smallpox and on a laboratory report that poxvirus particles have been demonstrated by electron microscopy. In any case, it should be limited to household and close contacts. WHO maintains a vaccine reserve which is intended for use if any unexpected emergency situation, confirmed by laboratory diagnosis, occurs in any country of the world.

### 8. Monkeypox (Annex 4)

Cases of monkeypox have occurred as a rare zoonosis in the areas of tropical rainforest in west and central Africa. The clinical picture of the disease cannot be distinguished from that of smallpox. The diagnosis can be made only by laboratory procedures. The risk of transmission is far less than with smallpox. If human monkeypox is suspected, it is most important to collect specimens for laboratory investigation and report the case to WHO which has special surveillance activities for this disease.

9. Relations with News Media

Smallpox rumours are always newsworthy. Experience shows that they have often been spread worldwide even before any investigation by national health authorities has been possible. If this happens health authorities must be prepared to deal with representatives of the media and the public in a calm and knowledgeable manner. International press agencies should be encouraged to contact WHO before disseminating reports of rumours. As far as national media are concerned, they should also be encouraged to contact their own national health authorities initially.

It is advisable for national health administrations to designate temporarily an information officer to coordinate the flow of pertinent information to the press, or the public if the rumour of a suspected smallpox case is causing substantial concern among the public. The assistance of WHO should also be sought in order to provide expertise on the evaluation of the case in question and to furnish general information on smallpox. It is useful to know that the last cases of endemic smallpox occurred in 1971 in South America, in 1972 in Indonesia, in 1975 in the Indian subcontinent and in 1977 in Africa.

## CLINICAL DIAGNOSIS OF SMALLPOX

1. Early Manifestations

The first manifestations of smallpox are fever, malaise, backache and headache. These continue for 2 to 3 days, following which the rash begins to appear. The rash is first noticed on the face and upper part of the body, but within a day or two involves the upper extremities and the lower extremities. From the third day after the appearance of the rash no new lesions appear. The rash is thus characterized as occurring in a single crop, and on any given part of the body the lesions are in the same stage of development.

Chickenpox, which was the disease most frequently confused with smallpox, develops in a different way. The pre-eruptive phase of the illness is milder and often not perceived at all. The fever is rarely high and the patient may not appear ill. The appearance of the earliest skin lesions is similar, but the lesions progress more rapidly through their successive stages of development. Furthermore, successive crops of new lesions appear over a week or more, so that at any given time there are lesions in different stages of development on any one part of the body.

Measles was the disease next most often confused with smallpox, because it causes fever and rash, and deaths are not uncommon in many developing countries. Measles, like smallpox, has a prodromal febrile phase, and the early macular or maculopapular rash may be like that of smallpox. However, when after a day or two, the lesions have not proceeded to become vesicles (i.e., do not contain free fluid) the diagnosis of smallpox can be ruled out. The same is true of the many other infectious diseases which cause fever and macular or maculopapular rashes.

2. Evolution of the Rash

On the first day of the rash small erythematous spots (macules) appear which, during the next one or two days, become raised above the skin's surface. These lesions are called papules. Fluid gradually accumulates in the papules, forming vesicles. The fluid in the vesicles then becomes cloudy and looks like pus. These lesions are called pustules. The vesicles and pustules are deeply seated, circular in shape with thick skin cover, firm to touch and can be rolled between the fingers without rupturing them. The pustular stage lasts for a varying period, usually between 7 and 10 days. Gradually the pustules dry up and form dark scabs which take one to two weeks to fall off, leaving depigmented areas. After several months the depigmented areas become hyperpigmented, appearing as dark spots. Eventually the skin returns to its previous appearance except for pitted scars (pockmarks) which are particularly noticeable on the face. In the more severe forms of smallpox the majority of persons who recovered had five or more facial pockmarks. Many had extensive facial scarring. There is no specific treatment for smallpox.

In chickenpox the rash evolves rapidly from maculopapular to vesicular (3 to 4 days) and to crusts in less than 10 days. The rash appears in crops, with new lesions appearing over a week or more. Thus the patient may have simultaneously macular, vesicular and other crusted lesions. The vesicular fluid usually is clear, with a thin covering of skin which ruptures easily with slight pressure. If secondary infection occurs, the vesicular fluid may become turbid and the lesions may look like smallpox pustules. The scabs are superficial and separate easily from the underlying skin. The skin rapidly returns to its normal appearance and it is unusual to have more than a few pockmarks on the face, almost never more than five in number.

Annex 1

3. Distribution of Rash (see Smallpox Recognition Card enclosed as insert)

This is one of the most important points in differentiating smallpox from other diseases with rash. The smallpox lesions are usually more abundant on the extremities and face than on the body (centrifugal distribution). In severe cases, the rash may cover the whole body. Another characteristic point is the presence of pocks on the palms and soles. The scabs from the lesions on the palms and soles fall off considerably later than they do from the lesions on the arms and legs.

In chickenpox the rash is more abundant on the body than on the extremities (centripetal distribution). The rash usually does not involve the palms and soles, but the occasional patient with a particularly heavy eruption may have lesions in those areas.

4. Periods of Communicability

Patients become infectious on the day before the appearance of the rash and remain infectious until the last scab has come off, usually for about 2 or 3 weeks. The patient transmits the infection most readily during the early stages of the rash.

5. Differentiation from Other Skin Diseases

Many other conditions with vesicular or pustular skin lesions have been misdiagnosed as smallpox in the past. These include generalized herpes and vaccinia, secondary syphilis, drug reactions, insect bites, scabies, impetigo, tanapox, molluscum contagiosum and erythema multiforme. The examiner who has seen smallpox will rarely have difficulty in distinguishing these from smallpox.



## EPIDEMIOLOGICAL INVESTIGATION

The health worker who encounters a suspected case of smallpox should search for any possible source of infection and should trace all possible contacts. The initial steps should be directed towards the patient, family or household and contacts.

### 1. The Patient

Basic data about the patient should be recorded. These include name, family name, age, sex, address, vaccination status and data of onset of rash. It is essential to obtain accurate dating of the onset of illness and to learn where the patient has been during the 3 weeks before the illness began. Vaccination status is important and a vaccination scar should be searched for. A listing should be made of all persons in the same household and of all contacts with any other persons with rashes, or with animals (if monkeypox is suspected), during this period. He should be asked specifically about chickenpox and any other diseases with rash which have recently occurred in the area. These questions should be asked again during subsequent daily visits in order to obtain information which might not have been recalled at the time of the first visit.

### 2. The Family or Household

A complete listing should be made of the patient's family and of all persons with whom he has shared a dwelling during the previous 3 weeks. Family or household members may provide information not known to or told by the patient, particularly if the patient is very young, is acutely ill or in the event that the patient has died. The questions are similar to those asked of the patient, namely, contact with other patients with fever and rash, chickenpox, pockmarks in persons who have had rash diseases in the recent past and recent deaths following acute illnesses. The use of smallpox recognition cards may be of help in eliciting information.

### 3. Other Contacts

All contacts should be seen and examined for evidence of recent rash disease or pockmarks. They should be questioned in the same manner as family and household members.

Inquiries of the sort outlined above will almost always eliminate the possibility of smallpox. However, in the rare situation where doubt persists, e.g. if other cases of a similar nature occur, more extensive village or neighbourhood investigations would be necessary. National health authorities, which by this time would have learned of the situation through the reporting system and would have received specimens from the suspected case, should at this point assume responsibility, since experienced personnel and extensive planning and resources are needed. These should be organized in consultation with WHO.

## COLLECTION AND DISPATCH OF SPECIMENS FOR LABORATORY DIAGNOSIS

Specimens collected for laboratory diagnosis are tested in WHO collaborating laboratories by two methods. Electron microscopy is used to demonstrate the presence of characteristic poxvirus particles in the specimen. It is more rapid than other methods. Culture on the chorioallantoic membrane of chick embryo is slower (several days) and less sensitive with older specimens but permits the differentiation between poxviruses which have identical appearances by electron microscopy, such as variola, vaccinia and monkeypox. Virus originally present in specimens may lose its viability if specimens are not kept at low temperatures and for this reason specimens should be refrigerated while awaiting dispatch. Vaccinia virus (vaccine) should not be opened in the same area where specimens are processed. There is a possibility that contamination may occur and a false diagnosis may be made by electron microscopy.

The very simple equipment shown in Figure 1 is sufficient for the collection and dispatch of specimens. Note that the specimen is dispatched in a triple container. The infected specimen is placed in the innermost container which is then placed in the second container. This is essential in order to meet the regulations for transporting infected specimens in commercial airlines. The third, or outer container, provides a further safeguard and helps to avoid breakage during shipment.

## 1. Collection of Specimens

### 1.1 Vesicular and pustular lesions

1.1.1 If capillary tubes are available, open the lesions with a sharp instrument such as a scalpel or hypodermic needle, fill 4 capillary tubes with fluid from the lesions and seal both ends of the tubes with plasticine. Put the capillary tubes in a test-tube or container and pack gently with cotton wool.

1.1.2 If no capillary tubes are available, open 3 or 4 lesions as described above and adsorb the contents on cotton swabs (Q-tips) wrapped around applicators. The base of the lesions should be vigorously swabbed, since there is more virus there than in the fluid. Place the swabs in a screw-capped container. If no such container is available, they may be placed in a test-tube. In this event the tube must be securely stoppered and wrapped with sticking plaster or tape.

### 1.2 Crusts (scabs)

With forceps, hypodermic needle or other sharp instrument take off as many crusts as possible. At least 10 should be collected and placed in a screw-capped container. Use a scalpel to rub across the base of the lesions and include the material collected in the container. Close the container by tightly screwing on the top.

Note: Because the containers contain potentially infectious material they must be securely closed and the outside should then be wiped with a disinfecting solution. The container should be clearly labelled with the name of the patient and date of collection of the specimen. All instruments used in collecting the specimens should be disinfected or autoclaved.

### 1.3 Convalescent or recovery stage

Serum collected following recovery may contain antibodies which are helpful in diagnosis. With a hypodermic needle and syringe or with a vacutainer collect 5 to 10 ml of blood. After coagulation of the blood and separation of serum at room temperature, the serum should be decanted with sterile procedures into 2 small plastic tubes. These tubes should be kept

in the freezer or refrigerator after labelling. Particular care should be taken to avoid haemolysis by handling the blood very carefully and keeping it still during the coagulation. Never freeze whole blood.

## 2. Packaging of specimens

- i) Put the specimen container (3)<sup>1</sup>, or stoppered, taped tube containing the specimens, in the screw-capped metal container (4) and fasten the lid tightly.
- ii) Fill the empty spaces along the bottom, sides and top with an adsorbent material.
- iii) Put the metal container (4) in the outer cardboard container (5). If cardboard cartons are not available use a box.
- iv) Include inside the outer container or box a form giving the following information on the patient: name, family name, age, sex, date of onset of rash, vaccination status and address.
- v) Be certain that the package is securely sealed.

## 3. Storage of specimens while awaiting dispatch

Specimens should be kept in a freezer or refrigerator and treated as contagious material.

## 4. Dispatch of specimens

The package should be sent as rapidly as possible to national public health headquarters which should forward it immediately to:

Smallpox Eradication Unit  
World Health Organization  
1211 Geneva 27  
Switzerland

In the case of specimens collected in the region of the Americas, these may be sent to:

World Health Organization  
Regional Office for the Americas/  
Pan American Sanitary Bureau  
525, 23rd Street, N.W.  
Washington, D.C., 20037  
United States of America

The package should be sent by airfreight, informing WHO by cable or telephone of the flight number, date and time of arrival and airway bill number. The WHO Programme Coordinator or WHO personnel within the country should be informed of this action and their assistance should be sought for safe dispatch of the specimen if required.

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<sup>1</sup> Numbers in brackets refer to the key beneath Figure 1.

## MONKEYPOX

### 1. Introduction

Human monkeypox is an acute exanthematous disease caused by monkeypox virus, a member of the orthopoxvirus group of poxviruses. Because the disease resembles smallpox, each suspected case merits a complete investigation.

### 2. Clinical Features

The signs and symptoms of monkeypox are similar to smallpox. Following a 7 to 15 day incubation period, there is a 2 to 3 day prodrome with fever, muscle and back pains and extreme fatigue. The various stages of rash develop over the face and body at about the same time; evolution of macules to papules, vesicles, pustules and finally scabs, takes about 10 days. Desquamation of scabs may take up to 3 weeks. Lesions are generally more concentrated on the extremities. The mucous membranes and cornea have been affected. Eight (16%) of the 51 reported cases have died. The differential diagnosis includes most commonly chickenpox, measles, bacterial skin infections, scabies, drug eruptions and syphilis.

### 3. Laboratory Diagnosis

Virus is present in the skin lesions. The virus is relatively stable, particularly in scabs. Laboratory confirmation requires that adequate material from virus-containing lesions be taken. Electron microscopy will show orthopoxvirus particles but cannot distinguish between members of the group. Culture on chorioallantoic membrane of chicken eggs can give a precise virus diagnosis in an experienced laboratory. Acute and convalescent sera help in the diagnosis if there is a titre rise; antibodies to specific orthopoxvirus can be detected by special testing in a WHO collaborating centre.

### 4. Epidemiological Features

From 1970, when the first case was found in Zaire, to December 1980, 51 cases of human monkeypox have been reported. All have been detected in tropical rainforest areas of central and west Africa, in the following countries: Zaire (40); Liberia (4); Nigeria (3); Cameroon (2); Ivory Coast (1); and Sierra Leone (1). Children less than 10 years of age have comprised more than 80% of cases. Five persons appear to have contracted the disease from an index case. The secondary transmission rate of human monkeypox to susceptible persons is 8% in close family contacts, and less than 4% for all susceptible contacts. This is much less than that of smallpox. No tertiary cases have been reported. Smallpox vaccination appears to protect against monkeypox. The natural reservoir of human monkeypox is unknown.

### 5. Treatment

There is no specific treatment for monkeypox. Attention should be given to adequate nourishment and hydration and to keeping the skin clean and dry. Antibiotics should be given to prevent secondary bacterial infection.

### 6. Prevention

Patients should be isolated in the village or hospital. Persons caring for the patient should have been successfully vaccinated against smallpox within the previous 3 years. A small group of health personnel in areas where monkeypox cases have occurred should be vaccinated and given the responsibility for investigating and caring for patients with monkeypox. Vaccination of the general population is not indicated even when a case is detected.

FIGURE 1  
EQUIPMENT FOR COLLECTION AND DISPATCH OF SPECIMENS  
FROM SUSPECTED SMALLPOX PATIENTS



1. Lancet
2. Sterile swabs
3. Plastic specimen collection container
4. Metal tin
5. Outer cardboard mailing container

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