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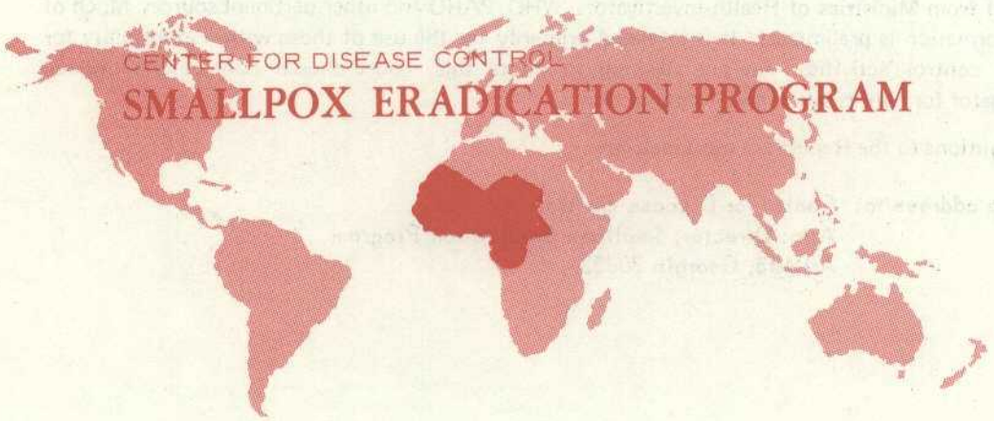
J D MILLAR, MD, ACTING DIRECTOR
STATE AND COMMUNITY SERVICES DIVISION
BLDG B, ROOM 207



CENTER FOR DISEASE CONTROL

SMALLPOX ERADICATION PROGRAM

SPECIAL REPORT

Human Infection with Monkeypox Virus: Liberia and Sierra Leone

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE

PREFACE

Summarized in this report is information pertaining to smallpox eradication and information received from Ministries of Health investigators, WHO, PAHO and other pertinent sources. Much of the information is preliminary. It is intended primarily for the use of those with responsibility for disease control activities. Anyone desiring to quote this report should contact the original investigator for confirmation and interpretation.

Contributions to the Report are most welcome.

Please address to: Center for Disease Control
Attn: Director, Smallpox Eradication Program
Atlanta, Georgia 30333

Center for Disease Control ..... David J. Sencer, M.D., Director

Smallpox Eradication Program ..... William H. Foege, M.D., Director

I. INTRODUCTION

The Regional Smallpox Eradication Program in twenty West and Central African countries has progressed with marked success since its beginning in 1967. There have been no confirmed smallpox cases since May 1970, when an outbreak was reported in Kwara State, Nigeria (SEP-R Volume IV, No. 5).

An active search has been made to establish the existence of non-human reservoirs of infections, especially in primates. Sixteen outbreaks of pox disease in monkeys have been summarized by Arita and Henderson.[1] This preliminary report presents the clinical, epidemiologic and laboratory investigations of four cases in Liberia and one case in Sierra Leone.

II. LIBERIA

A. Background

On September 17, 1970, The Liberian National Public Health Service received a radio report from the Medical Officer in Zwedru, Grand Gedeh County (Figure 1) of the hospital admission of a smallpox case on September 14. An investigator flew to Zwedru on September 18, to initiate an investigation.

Zwedru, the capital of Grand Gedeh County, has a population of 5,200 with 63,000 residing in the county as a whole. The county is bordered on the northeast by the Ivory Coast, on the northwest by Nimba County, on the southwest by Sinoe County, and on the south by Maryland County. There is one main road which bisects the county in a northwest to southeast direction. About 1/3 of the population lives along this motor road, which was constructed during 1959-1962. Three main tribes live in the county: The Khron in the northwest, the Graebo in the southeast, and the Mandingo in the cities and towns.

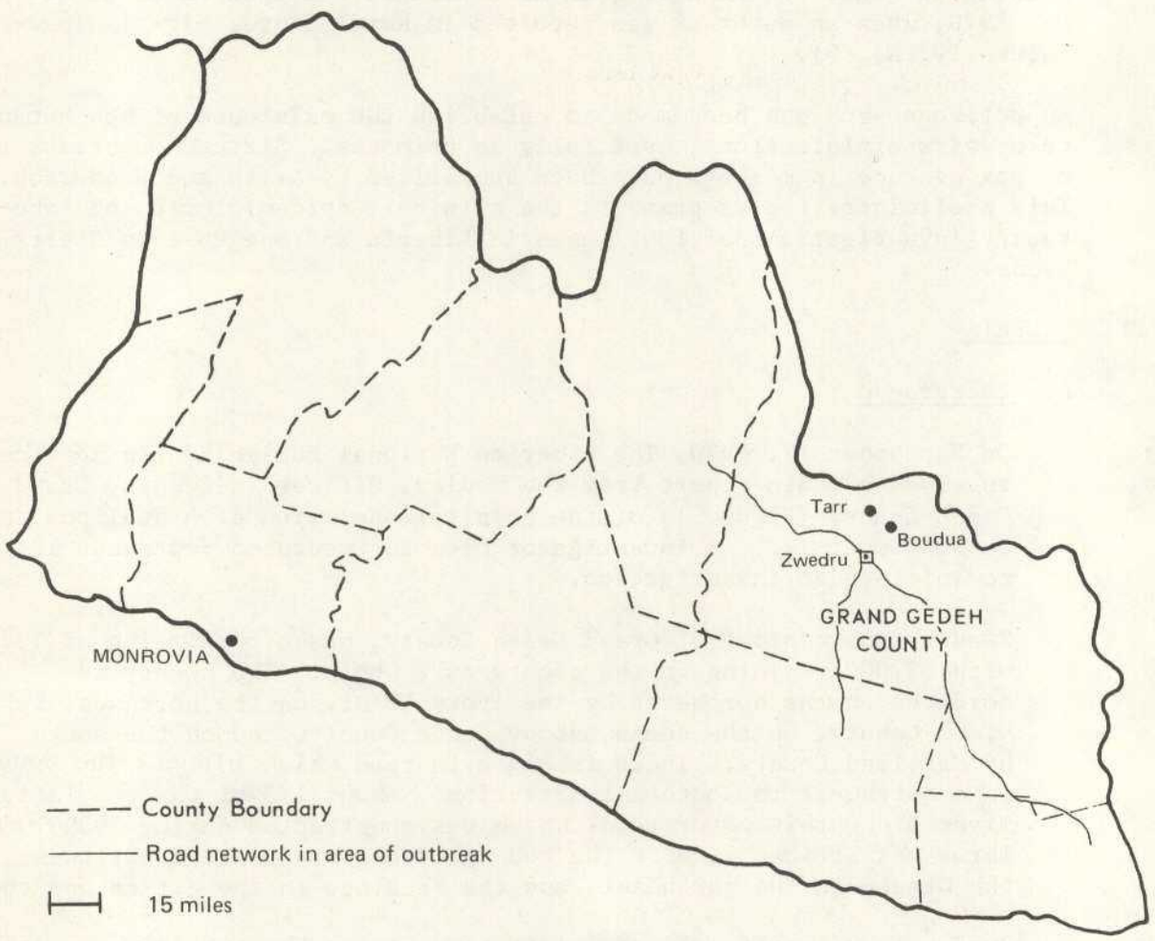
Zwedru is a trading and administrative center for the county and has a hospital whose medical officer is responsible for all preventive and curative services in the county.

Grand Gedeh County has large timber reserves which have recently been opened for selective cutting. The predominant cash crops grown in the area are coffee and cocoa. The staple crop is rice which is grown in upland fields located deep in the forest. The farmers generally live in small villages and towns of less than 100 people that are scattered throughout the forest. These are grouped into homogenous tribal groups called clans, each ruled by a clan chief. In addition to their homes in the villages, the farmers often have a second home on their farm several hours walk from their village.

[1] Arita, I. and Henderson, D.A.: 1968 Bull. Wld. Hlth. Org. 39: 277-283.

Figure 1

Map of Liberia Showing the Area of the Monkeypox Outbreak
September - October 1970



Grand Gedeh County was last systematically vaccinated in 1962, when the Brother's Brother vaccination campaign vaccinated most of the villages in the county. The last year that Grand Gedeh County had a confirmed outbreak of smallpox was 1962. This outbreak was particularly severe in Kannah Clan of Tchien administrative area, but cases also occurred in other areas in the county. About 5,500 vaccinations were performed in Zwedru city during November 1968, when the President's birthday celebration was held in Zwedru.

B. The Investigation

1. Epidemiology

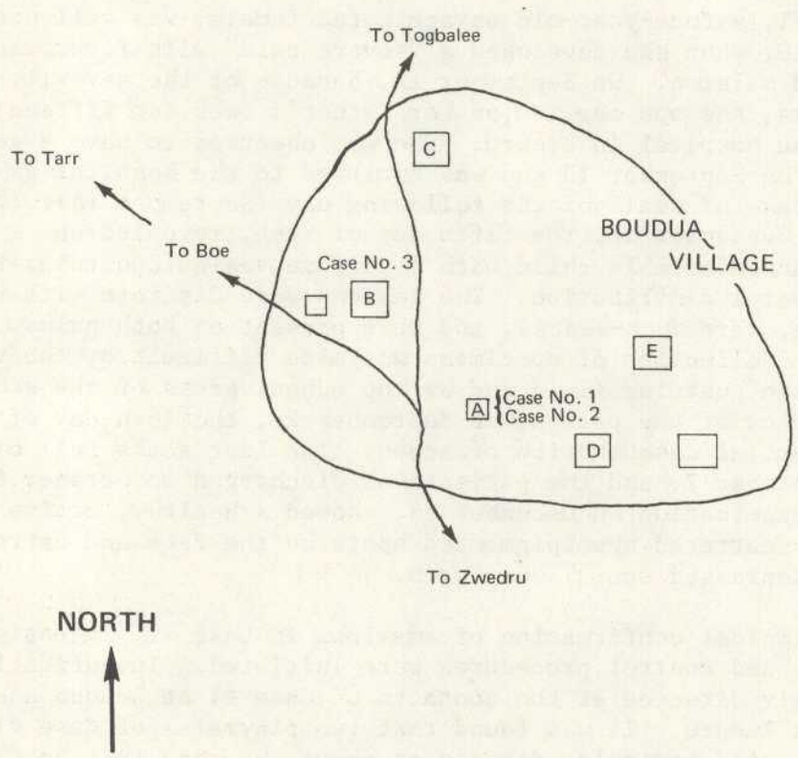
Case #1, a four-year-old unvaccinated female, was well until September 10, when she developed a "severe cold" with fever, sore throat, and malaise. On September 12, because of the severity of her symptoms, she was carried on her father's back for fifteen miles to the hospital in Zwedru. She was observed to have a generalized rash on September 13 and was admitted to the hospital as a suspected case of smallpox the following day (September 14). Examination on September 18, the fifth day of rash, revealed an afebrile, uncomfortable child with a diffuse vesiculopustular rash with peripheral distribution. The lesions were discrete with rare coalescence, were deep-seated, and were present on both palms and soles. Collection of specimens was made difficult by the viscosity of the pustular fluid and by the adhesiveness of the scabs. Re-examination of the patient on September 28, the 15th day of rash, revealed partial desquamation of scabs. The last scabs fell off on or about October 7, and the patient was discharged on October 8. Follow-up examination on December 13, showed a healthy, active child with scattered hyperpigmented spots on the face and extremities. No pocks (depressed scars) were seen.

With the clinical confirmation of smallpox in Case #1, intensive investigative and control procedures were initiated. Investigation was initially directed at the contacts of Case #1 at Bouduo and the hospital in Zwedru. It was found that two playmates of Case #1, had developed a mild vesicular disease at about the same time as Case #1.

Cas #2, a four-year-old unvaccinated boy, lived in Compound A in the same hut and room with Case #1 (Figure 2). On September 11, he developed a low-grade fever but was not acutely ill. On the evening of September 12, he developed a mild vesicular rash consisting of approximately ten scattered lesions. These lesions cleared completely in 3-5 days and left no scars or pigmentary changes. When subsequently challenged with vaccinia, no reaction occurred.

Figure 2

Boudua Village, Liberia



Case #3, a six-year-old unvaccinated female (a playmate of Case #'s 1 and 2), lived in Compound B in Bouduo. She had a mild illness consisting of a 2-3 day febrile prodrome followed by a 3-5 cay episode of rash. There were less than 10 lesions with no definite distribution. She had no response to post illness vaccination.

No history of contact with a person with a rash illness could be obtained from the families of these three patients. All had resided in Bouduo town continuously from 28 August 1970, to the onset of their rash. Case #2 had traveled with his grandmother to Zwedru on 20 August, and returned on 28 August. From September 10-17 many visitors from the clan had come to Bouduo in connection with the death of the great grandmother of Case #1 who died on September 9. The illness was enteric in nature and reportedly had no rash or hermorrhagic phenomena. None of these visitors stayed in Compound A where Case #'s 1 and 2 lived; however, many stayed in Compound B which was owned by the acting town chief and where Case #3 became ill.

Case #4, a nine-year-old unvaccinated boy from Tarr Town, developed rash on October 2, and was isolated on the family farm. When examined on October 10, the ninth day of rash, the boy had a general vesiculopustular rash with all lesions appearing in the same stage. The lesions were firm, deep-seated, and measured approximately 0.75 cm in diameter. Lesions on the face and lower extremities had been broken by local treatment. Lesion density was greatest on the arms and legs with slightly fewer lesions on the face. Scattered lesions were noted on the back and abdomen with increased density over the buttocks. Lesions were noted on both the palms of the hands and the soles of the feet. Some of the palmer and all of the planter lesions were very deep and did not appear above the skin surface. The patient had a tender warm mass in the right submaxillary area with swelling of the right side of his face and the orbit. An active pustular lesion was present in the right cornea. The child was uncomfortable but afebrile and not severely ill. Collection of pustular fluid was difficult because of high fluid viscosity. Scab removal caused slight bleeding at the base. The submaxillary abscess was treated with penicillin. Follow-up examination on October 26, the 25th day of rash, showed areas of depigmentation, a right corneal scar and a subsiding submaxillary mass. The areas of depigmentation were again noted on November 20. Re-examination on December 16, revealed a 4-5 mm right corneal scar. It was not possible to differentiate any clear pattern of pigmentary change at that time.

Exposure to anyone with a rash for a period of three weeks prior to his illness was denied. Case #4 had not been out of Tarr Town for at least three months except to go to his father's farm. His family specifically denied any travel or contact with anyone from Bouduo. One family had come from Zwedru to attend the funeral of Case #4's aunt who died 14 September, but none of the people coming from Zwedru had any contact with Case #1, who was in the Zwedru hospital at that time. The aunt's death was reportedly due to post-partum hemorrhage. Many people attended this funeral from the villages surrounding Tarr town, but none came from Tchien Mehyah clan where Case #'s 1, 2 and 3 had occurred. The village elders denied that any of the mourners had a rash illness.

Table 1 shows all residents present in Bouduo town during mid-September by vaccination status. Of the 26 permanent residents surveys, 13 had no vaccination scar prior to the outbreak of pox illness. Three of these developed a pox illness while the other 10 did not. These ten were all successfully vaccinated during the epidemic control measures on September 28 and 29, (fifteen days after onset of rash in Case #'s 1, 2 and 3). A village-by-village surveillance vaccination program was initiated in Tchien Mehyah and adjoining clans in the expectation of uncovering undetected smallpox transmission. Vaccination scar rates as assessed during active surveillance are also presented in Table 1. Through these active surveillance efforts, Case #4 was detected in Tarr Town of Niabo Clan.

In order to determine the full scope of this outbreak and to determine the possible source of infection, an intensive, active surveillance program was organized in the three western districts in Grand Gedeh County (Gbarzon District, Tchien Administrative area, and Konobo District). The investigators were given a complete list of all villages and towns that were in their clans and asked to survey these villages for recent pock disease, immunity status, and smallpox scarring. A search was made for anyone who had a history of smallpox within the last year or for new cases of smallpox. In addition, the schools in Zwedru and those along the motor road were contacted and the investigators were asked to report smallpox cases. Fifteen cases of pock disease occurring in the last year were reported by the investigators. In follow-up investigation, varicella or other non-pox diseases was identified in each case.

From a total of 19,025 people examined in the active surveillance program, 13,576 had a vaccination scar for a rate of 71.3 percent. The post epidemic control vaccination scar rates by clan are presented in Table 2. There is considerable variation in these rates, ranging from a low of 34.8 to a high of 99.3. However, the immediate area of the outbreak showed scar rates of 99.3 (Niabo) and 95.5 (Tchien Mehyah).

Table 1

Smallpox Vaccination Status of Bouduo and Togbalee Towns, Zwedru Town and Niabo Clan
Grand Gedeh County, Liberia, October, 1970

Age Group	Sex	Bouduo			Togbalee			Zwedru			Niabo Clan		
			Vaccinated			Vaccinated			Vaccinated			Vaccinated	
		Sample	Number	Percent	Sample	Number	Percent	Sample	Number	Percent	Sample	Number	Percent
0-4	Male	3	0	-	3	1	33.3	83	21	25.3	116	12	10.3
	Female	3	1	33.3	10	0	-	81	14	17.3	83	12	14.5
	Total	6	1	16.7	13	1	7.7	164	35	21.2	199	24	12.0
5-14	Male	1	0	-	11	4	36.4	161	120	74.5	93	39	42.0
	Female	3	0	-	9	2	22.2	160	120	75.0	98	46	47.0
	Total	4	0	-	20	6	30.0	321	240	74.8	191	85	44.5
15+	Male	4	4	100.0	33	24	72.7	258	173	67.1	130	108	83.1
	Female	12	9	75.0	37	22	59.5	327	211	64.5	198	164	82.8
	Total	16	13	81.3	70	46	65.7	585	384	65.6	328	272	83.0
Total	Male	8	4	50.0	47	29	61.7	502	314	62.6	339	159	46.9
	Female	18	10	55.6	56	24	42.9	568	345	60.8	379	222	58.5
	Total	26	14	53.8	103	53	51.5	1070	659	61.5	718	381	53.0

Table 2

Vaccination Scar Rate (%) as Determined After Epidemic Control Measures, Grand Gedeh County, Liberia December, 1970

Clan	Vaccination Scar Rate (%)
Bhai	78.0
Gbaeboe	60.7
Gbarboe	61.0
Gbarlo	34.8
Gborboe	83.1
Kannah	81.2
Krazon	84.4
Neezonie	88.3
Niabo	99.3
Tchien Mehyah	95.5
Tchien Meson	65.9

2. Laboratory Results

Five separate pox virus isolations have been obtained from specimens submitted from Case #'s 1 and 4 (Table 3). Case #'s 1 and 4 were the more severe cases.

Table 3

Pox Virus Isolates from Grand Gedeh County, Liberia, 1970

Case #	Material	Date	EM[1]	AG[2]	CAM[3]
1	Skin	9/18	+	+	Small Hemorrhagic Pocks
	Fluid	9/18	+	ND[4]	Small Hemorrhagic Pocks
	Crusts	9/23	+	+	Small Hemorrhagic Pocks
	Fluid	9/23	+	NS	Small Hemorrhagic Pocks
4	Crust	10/7	-	-	Negative
	Fluid	10/7	+	ND	Small Hemorrhagic Pocks
	Crusts	10/10	-	-	Negative

[1] EM - Electron Microscope
[2] AG - Agar Gel precipitation test for pox antigen
[3] CAM - 12 day embryonated hens eggs-chorioallantoic membrane at 72 hours
[4] ND - Not done

Pox virus isolates of Case #'s 1 and 4 have been intensively studied at CDC in Atlanta. Similar studies are being carried out by Marennikova in Moscow, Dumbell and Rondell in London and Gispen in Utrecht. Reference viruses have included three monkeypox strains, Utrecht (65-32), McConnel, Copenhagen; three variola strains, Harvey, Butler, Niger (68-12); and vaccinia (Wyeth).

The Liberian isolates produce small pocks with central necrosis and hemorrhage when inoculated onto the chorioallantoic membrane. The lesions resemble those produced by the Utrecht, Copenhagen and McConnell strains of monkeypox and differ from those produced by Harvey variola, the latter being slightly larger and having no central necrosis or hemorrhage.

When inoculated into monkey kidney tissue culture (VERO and LLC-MK_2 cells), the Liberian isolates produced large plaques similar to those of the three monkeypox strains, but distinctly different from those produced by strains of variola.

Like monkeypox, the Liberian isolates grow at 39°C, variola does not.

The Liberian isolates are much more lethal for chick embryos and suckling mice than is variola, which is a characteristic of monkeypox. The most dramatic difference between the Liberian isolates and variola is in its growth in rabbits. Variola causes a minimal pink lesion when inoculated intradermally - it cannot be successively passed in rabbit skin. Vaccinia causes a local lesion but no systemic disease. Both the Liberian isolates and monkeypox produce large necrotic, hemorrhagic local lesions and a generalized illness with florid secondary exanthem. The virus is easily recovered from the secondary lesions and passes easily in rabbit skin.

To confirm the uniqueness of these isolates, 44 African strains isolated since 1968 have been re-examined. All were inoculated into rabbits and 15 were inoculated into eggs and tissue culture. All behaved like variola.

These studies identify a pox virus which differs from variola, vaccinia, rabbitpox, mousepox and cowpox and which is indistinguishable from monkeypox.

C. Source of Infection

With the identification of a non-variola pox virus, investigations were launched in December 1970 for a non-human source of infection.

Hunters reported a gradual decrease in available game (duiker, monkey) in the area of Bouduo but denied any evidence of animal die-off. No abnormal skin lesions were noted in recent kills. Due to the absence of hunters from Bouduo in early September, no game was killed in the two weeks prior to the onset of the illness of Case #'s 1, 2 and 3. During that period of time smoked meat was used. In addition to wild animals, the villagers have frequent contact with domestic livestock including goats, sheep, dogs, cats, and poultry. Exposure of the infected children to domestic animals and to butchering (wild and domestic) was observed. Through cooperation with the village chief and the village hunters, serologic specimens were obtained from 18 monkeys. The serologic results are presented in Table 4.

Table 4

Hemagglutination Inhibition Titers of 18 Monkey Sera Collected from Grand Gedeh County, Liberia

Monkey Species	Number	HI Titer <8	8
Spot	5	3	2
Mono	5	5	
Red	1	1	
Green	1	1	
Black	1	1	
Diana	2	1	1
Grey	1		1
Stampfli	1		1
Potto	1	1	

The five monkey sera with HI titers of 8 were also tested by vaccinia plaque reduction neutralization. One of them, a spot monkey from Tarr, had a titer of 1:30, the others were negative.

D. Discussion

Human infection with a pox virus similar to the described monkeypox is a previously unrecognized illness. Two similar cases are currently under investigation, one in the Congo and the other in Sierra Leone. As reported in this paper, the severe form of the disease is characterized by a 2-3 day prodrome, a vesiculopustular rash indistinguishable from that of smallpox, and recovery without scarring.

Animal experiments have shown cross protection between variola, vaccinia, and monkeypox. This is supported by the failure of these four cases, all unvaccinated,to respond to post illness challenge with vaccinia virus. The susceptible population among contacts of infected cases can be estimated as those individuals without history or evidence of smallpox or vaccination. Fifteen individuals were identified who had potential exposure to the infected cases. None of these developed disease and all developed a primary reaction to vaccination.

A three-year-old unvaccinated girl who was vaccinated four days after exposure had prolonged exposure to the more severe cases (Case #'s 1 and 4). Also, a 45-year-old unvaccinated female, took care of Case #1 during her prodrome and also took care of Case #2 during his period of illness. None of the remaining susceptibles had prolonged or intimate exposure to the more severe cases.

As the onset of illness for Case #'s 1, 2 and 3 was simultaneous, a common exposure is postulated. In view of the lack of contact between Bouduo and Tarr, it is also probable that Case #4 represents a separate exposure. From the collected data, there is no evidence which suggests that this disease can be transmitted from human to human.

The source of infection is not known. In none of the cases can exposure to a sick animal be documented. Based on the past known isolation of monkeypox virus from monkeys, a monkey source for the disease is postulated, but other animal sources cannot be excluded.

A major unanswered question is whether these cases represent the development of a new disease entity, or whether they represent the recognition of a previously existent disease entity. Evaluations of smallpox surveillance in West Africa have identified a surveillance efficacy of approximately 5 percent prior to the Regional Program. Thus, previous reporting would identify only 1 in 20 cases. In the past, reporting and investigation have been directed at outbreaks and little attention has been given to single cases. As part of the national smallpox eradication program, surveillance systems have been improved and the investigation of every suspect case including laboratory evaluation has become a matter of policy. Thus, the changes in the surveillance system could account for the new recognition of a low frequency human infection. A single report from the Congo in 1940 is suggestive of human infection with monkeypox virus. Material obtained from a case of "alastrim" produced cutaneous infection when inoculated into rabbits. Based on the known pathogenicity of monkeypox virus for rabbits, this could in retrospect have been the first recognized case of human monkeypox.

E. Summary

Four human infections of a pox virus similar to monkeypox occurred in September and October 1970, in Grand Gedeh County, Liberia. Epidemiological data suggests the accidental infection of humans from animal sources. No evidence for human transmission was uncovered. Low level antibody titers against pox viruses of the vaccinia group were identified in certain species of monkeys from the same area.

III. SIERRA LEONE

A. Background

On December 9, 1970, a suspected case of smallpox was reported to the Ministry of Health in Freetown from the Medical Officer in Moyamba District Hospital. An investigation was begun the next day. The patient lived in Aguebu (Figure 3), a small village four miles east of Moyamba. There are seven thatched roof, mud houses in the village; six of which were occupied at the time of the investigation. Vegetation in the area consists mainly of palm, banana, and paw-paw trees, with rice and cassavas cultivated for consumption. The villagers also purchase monkeys from hunters for meat consumption. The primary source of income in the village is the collecting and selling of palm wine.

B. The Investigation

1. Epidemiology

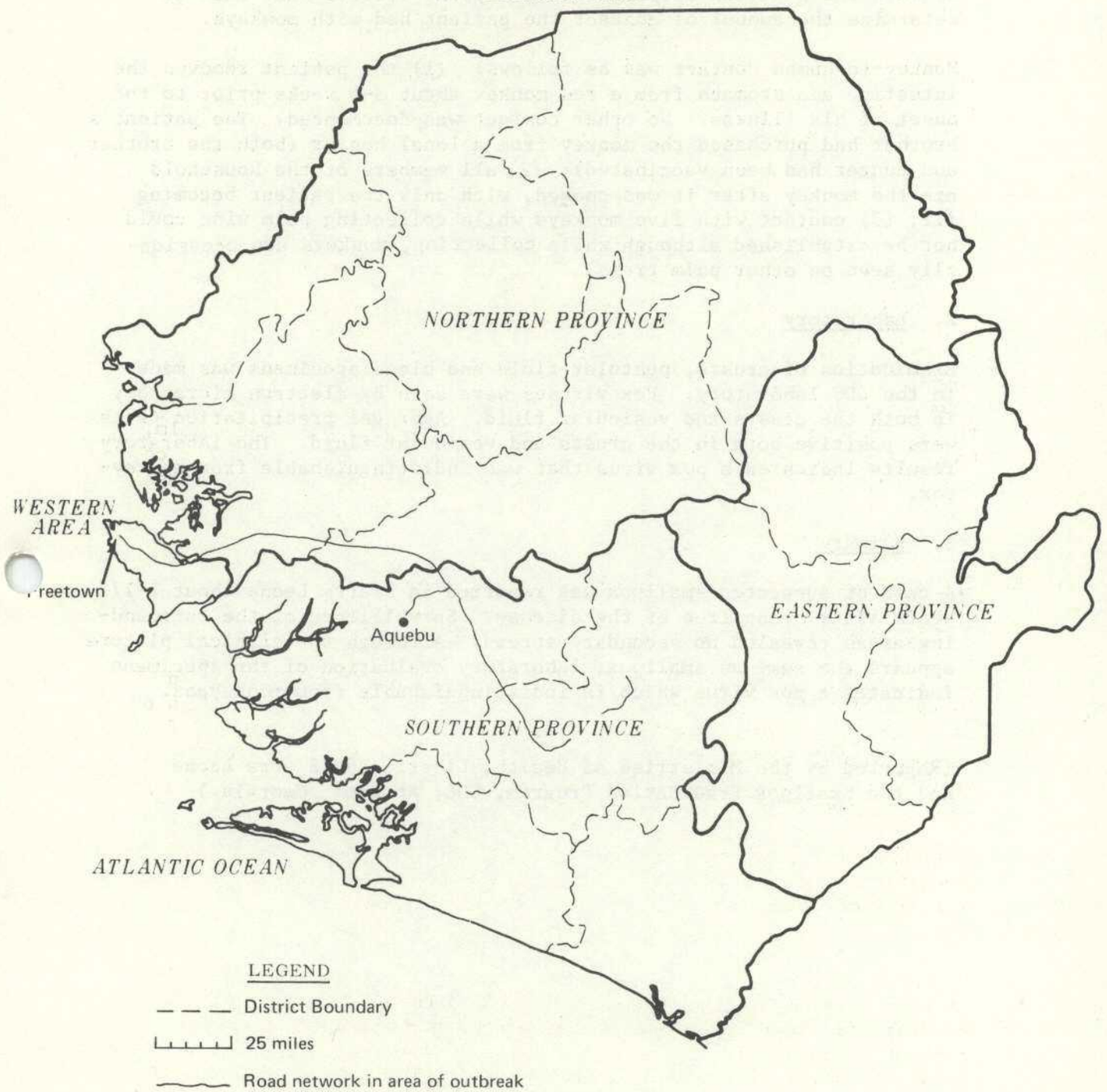
The patient, a 24-year-old unvaccinated male, developed a rash on December 1, 1970. He had no known exposure to anyone with a rash or other acute illness. During the prodromal period he experienced fever, headache, stiff neck, sore throat and cough.. He was seen on the fifth day of rash at the Moyamba Hospital, where he was treated with calamine lotion and sent back to his village.

A second visit, made on the 10th day of rash, revealed many large pustular lesions on his extremities and face. Based upon the history and physical examination, the patient was diagnosed as having smallpox.

Contacts of the patient were as follows: (1) six other people living in the household where the patient resided (three of these had no vaccination scars nor previous history of vaccination); (2) the patient's brother in the nearby village of Masonesi with whom he had spent the night just prior to his illness; (3) other individuals at the Moyamba Hospital with whom the patient had contact while waiting to be examined; (4) three people who cared for him during his illness and (5) other members of his village with whom casual contact could be identified (13 of the 29 residents had not been vaccinated). In none of these contact situations was transmission of the disease identified.

Figure 3

Map of Sierra Leone Showing the Area of the Monkeypox Outbreak
December 1970



As with the Liberian outbreak of monkeypox, efforts were made to determine the amount of contact the patient had with monkeys.

Monkey-to-human contact was as follows: (1) the patient removed the intestine and stomach from a red monkey about 3-4 weeks prior to the onset of his illness. No other contact was documented. The patient's brother had purchased the monkey from a local hunter (both the brother and hunter had been vaccinated); (2) all members of the household ate the monkey after it was cooked, with only the patient becoming ill; (3) contact with live monkeys while collecting palm wine could not be established although while collecting, monkeys are occasionally seen on other palm trees.

2. Laboratory

Examination of crusts, pustular fluid and blood specimens was made in the CDC laboratory. Pox viruses were seen by electron microscopy in both the crusts and vesicular fluid. Agar gel precipitation tests were positive both in the crusts and vesicular fluid. The laboratory results indicated a pox virus that was indistinguishable from monkeypox.

3. Summary

A case of suspected smallpox was reported in Sierra Leone about 1-1/2 years after being free of the disease. Surveillance of the surrounding areas revealed no secondary spread. Although the clinical picture appears the same as smallpox, laboratory evaluation of the specimens indicates a pox virus which is indistinguishable from monkeypox.

(Reported by the Ministries of Health, Liberia and Sierra Leone and the Smallpox Eradication Program, CDC, Atlanta, Georgia.)