Update
Le point

Articles in the ***Update*** *series give a concise, authoritative, and up-to-date survey of the present position in the selected fields, and, over a period of years, will cover many different aspects of the biomedical sciences and public health. Most of the articles will be written, by invitation, by acknowledged experts on the subject.*

Les articles de la rubrique ***Le point*** *fournissent un bilan concis et fiable de la situation actuelle dans le domaine considéré. Des experts couvriront ainsi successivement de nombreux aspects des sciences biomédicales et de la santé publique. La plupart de ces articles auront donc été rédigés sur demande par les spécialistes les plus autorisés.*

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Human monkeypox, 1970–79*

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Increasing attention has been given to human monkeypox since the achievement of global smallpox eradication. Monkeypox, which was first described in Central Africa in 1970, resembles smallpox clinically but differs from it epidemiologically. Forty-seven cases of human monkeypox have occurred since 1970 in 5 Central and West African countries; 38 of these cases have been reported from Zaire. The evolution of the illness and the sequelae of monkeypox and smallpox are the same; monkeypox has a case-fatality rate of about 17%. Children below 10 years of age comprise 83% of the cases. All cases have occurred in tropical rainforest areas and clustering of cases has been observed in certain zones within countries and within families. Person-to-person spread may have occurred in 4 cases; the secondary attack rate among susceptible, very close family members was 7.5% (3 cases/40 contacts) and among all susceptible contacts was 3.3% (4 cases/123 contacts)—much lower than the 25–40% secondary attack rate that occurs with smallpox. Although the low transmission rate and the low frequency of disease indicate that monkeypox is not a public health problem, more data are needed.

Whilst many animals near human monkeypox cases have been demonstrated to have orthopoxvirus antibodies, the natural reservoir(s) and the vector(s) of monkeypox virus are unknown. Studies are in progress to identify the natural cycle of monkeypox virus and to define better the clinical and epidemiological features of this disease.

Monkeypox was first discovered in man in Basankusu district, Equateur Region, Zaire, in 1970, 2 years after the last case of smallpox had occurred in the area. It is a disease that resembles smallpox clinically, but which differs from it in important epidemiological aspects. Some features of the first 21 human monkeypox cases have been reviewed earlier.[a] This report describes the clinical and epidemiological characteristics of all the 47 cases of human monkeypox reported from 1970 up to the end of 1979.

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* A French translation of this article will appear in a later issue of the *Bulletin*.

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[a] LADNYI, I. D. ET AL. *Bulletin of the World Health Organization*, **46**: 593-597 (1972); MARENNIKOVA, S. S. ET AL. *Bulletin of the World Health Organization*, **46**: 599-611 (1972); FOSTER, S. O. ET AL. *Bulletin of the World Health Organization*, **46**: 569-576 (1972); ARITA, I. & HENDERSON, D. A. *Bulletin of the World Health Organization*, **53**: 347-353 (1976); BREMAN, J. G. ET AL. *American journal of tropical medicine and hygiene*, **26**: 273-281 (1977).

As global eradication of smallpox has now been achieved, and most countries have stopped vaccination, immunity levels in the population will soon decline rapidly; it thus is extremely important that diseases resembling smallpox be carefully evaluated. Such investigations are essential to provide continuing assurance to health officials and the public alike that smallpox has indeed been eradicated and that vaccination is no longer necessary.

CLINICAL FEATURES

The major clinical features of human monkeypox are similar to those of smallpox. There is a 2–4-day prodromal illness with fever and prostration before the eruption begins. As with smallpox, the lesions develop more or less simultaneously and evolve together at the same rate through papules, vesicles, and pustules before umbilicating, drying, and desquamating. This process usually takes about 2–4 weeks, depending on the severity of the disease. The distribution of the rash is mainly peripheral. Severe eruptions may cover the entire body (Fig. 1–6), including the palms and soles. Six (13%) of the 47 known cases had a mild illness (less than 25 lesions, with no incapacity, not usually requiring medical care), 18 (38%) had moderate disease (more than 25 lesions, with moderate incapacity, usually requiring medical care), and 23 (49%) had severe disease (more than 100 lesions, severe incapacity, requiring medical care) (Table 1).

Most skin lesions are about 0.5 cm in diameter but some up to 1 cm have been seen. Lesions have been noted on the mucous membranes, the tongue, and the genitalia (Fig. 4 and 6). Lymphadenopathy, especially in the neck (submandibular and cervical) and the inguinal areas, was particularly prominent in 18 cases (Fig. 4 and 5).

Pitting scars develop most frequently on the face, and diminish with time. Secondary infection of the lesions is common and may play a role in scarring. About half of the scars from lesions seen initially on the face and body were detectable 1–4 years after the acute illness. Desquamation of crusts leaves areas of hypopigmentation. Hyperpigmentation follows after a few months and diminishes with time (Fig. 7). In some cases, large shallow residual scars are seen. In one case a primary corneal lesion caused unilateral blindness (Fig. 8). Another patient who was vaccinated several years previously developed only 1 lesion (Fig. 9) further emphasizing that some cases can be exceedingly mild and may go unreported.

Only 4 of the 47 patients (9%) had a vaccination scar. These were persons, aged 35, 30, 24, and 8 years, who had been vaccinated more than 5 years previously.

Eight (17%) of the patients died from monkeypox during the acute illness. They were between 7 months and 7 years of age. None had been vaccinated. Three other patients died of other causes 2 months, 4 months, and 14 months, respectively, after their illness.

Comparatively few laboratory tests have been done on these patients, mainly because of delays in reaching the patient after notification, difficulties in collecting scrapings from lesions or obtaining serum, and problems in procuring follow-up samples.

Table 2 gives virological and serological test results. For the 47 patients, monkeypox virus isolation confirmed the diagnosis in 30 out of 39 patients from whom skin scrapings were taken. Poxvirus particles were seen on electron microscopic (EM) examination of skin samples from 7 others, but virus was not isolated. Ten others had serological as well as clinical and epidemiological evidence of monkeypox infection; skin specimens were not collected from seven of these patients, and another specimen was not suitable for testing.

The virus could be isolated from specimens taken up to 18 days after onset of the rash. A specimen from 1 patient (case 19) which was EM-negative, was positive for monkeypox virus upon culture. The precipitation-in-gel test was less helpful than other virological methods; in no instance was the test positive when EM and/or culture were negative.

Table 1. Human monkeypox cases in West and Central Africa, 1970–79

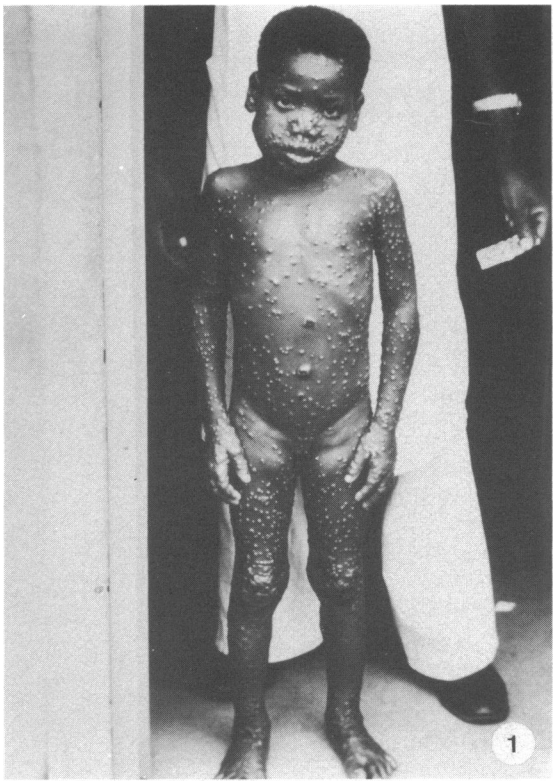
Case no.	Village name[a]	Region/ County, etc.	Country	Age (years)	Sex	Vaccination scar	Date of onset of rash	Severity[b]	Death	Comments
1	Bokenda	Equateur	Zaire	9/12	M	–	24.8.70	2	–	Died of measles after 2 months
2	Boudua	Grand Geddah	Liberia	4	M	–	12.9.70	2	–	
3	Boudua	Grand Geddah	Liberia	4	F	–	13.9.70	1	–	Aunt of, and co-primary with case 2
4	Boudua	Grand Geddah	Liberia	6	F	–	13.9.70	1	–	Co-primary with case 2; in adjacent house to cases 2 and 3
5	Tarr Town	Grand Geddah	Liberia	9	M	–	2.10.70	2	–	
6	Limba Corner	Açuebu	Sierra Leone	24	M	+	1.12.70	2	–	
7	Ihie Umduru	Aba	Nigeria	4	F	–	9.4.71	3	–	
8	Ihie Umduru	Aba	Nigeria	24	F	–	18.4.71	1	–	Secondary transmission presumed; mother of case 7
9	Bosmatché	Abengourou	Ivory Coast	5	M	–	18.10.71	2	–	
10	Ilonga	Kasai Oriental	Zaire	1	M	–	2.3.72	2	–	
11	Libela (B)	Equateur	Zaire	3	M	–	27.7.72	3	+	
12	Yamileka (B)	Equateur	Zaire	30	F	+	27.7.72	1	–	Mother of, and co-primary with case 11
13	Bokokolo	Equateur	Zaire	7/12	F	–	16.9.72	3	+	
14	Niangi	Bandundu	Zaire	2	M	Doubtful	30.10.72	3	+	
15	Bogon	Equateur	Zaire	3	F	–	10.1.73	2	–	
16	Bogon	Equateur	Zaire	5	F	Doubtful	22.1.73	2	–	Secondary transmission presumed; sister of case 15
17	Bombana (B)	Equateur	Zaire	7/12	M	–	6.5.73	3	+	
18	Bumba Town (B)	Equateur	Zaire	4	F	Doubtful	6.8.74	2	–	
19	Iba	Bandundu	Zaire	40	F	–	4.2.75	3	–	
20	Djungula (K)	Kasai Oriental	Zaire	23	F	–	9.3.75	1	–	
21	Ebata (B)	Equateur	Zaire	2	F	–	4.3.76	2	–	
22	Yangomba (B)	Equateur	Zaire	7	M	–	7.6.76	3	–	
23	Masina	Bandundu	Zaire	8	F	+	27.8.76	3	–	
24	Yamagbe-Bohumbe (B)	Equateur	Zaire	7	F	–	12.2.77	3	–	
25	Iwadji (K)	Kasai Oriental	Zaire	4	M	–	12.2.77	2	–	
26	Yabokungu-Bohumbe (B)	Equateur	Zaire	8/12	F	–	4.3.77	2	–	No contact with case 24; died of ? after 14 months
27	Yamagbe-Bohumbe (B)	Equateur	Zaire	35	F	+	7.3.77	1	–	Mother of, and co-primary with case 26
28	Bwalayulu	Bandundu	Zaire	1	M	–	14.3.77	2	–	
29	Katanti	Kivu	Zaire	4	F	–	22.3.77	3	–	
30	Manzita	Bandundu	Zaire	14	M	–	4.1.78	3	–	
31	Ikela	Equateur	Zaire	7	M	–	5.2.78	3	+	
32	Mongo Senge (K)	Kasai Oriental	Zaire	4	F	–	16.2.78	3	–	
33	Mongo Senge (K)	Kasai Oriental	Zaire	6	M	Doubtful	18.2.78	2	–	Brother of, and co-primary with case 32; died of malnutrition after 4 months
34	Imbimbi	Bandundu	Zaire	5	F	–	6.5.78	3	+	
35	Okela (K)	Kasai Oriental	Zaire	2	M	–	11.9.78	3	+	
36	Ekodji (K)	Kasai Oriental	Zaire	6	F	–	28.9.78	3	–	Secondary transmission presumed; cousin of case 35
37	Mindembo (B)	Equateur	Zaire	3	F	–	9.11.78	2	–	
38	Mindembo (B)	Equateur	Zaire	1	M	–	16.11.78	3	–	Brother of, and co-primary with case 37
39	Omifounfoun	Oyo	Nigeria	35	M	–	22.11.78	2	–	Reported from Parakou, Benin
40	Yaliengo (B)	Equateur	Zaire	7	F	–	23.11.78	3	–	
41	Apoko (K)	Kasai Oriental	Zaire	3	M	–	11.12.78	3	–	
42	Yamahonde (B)	Equateur	Zaire	3	M	–	6.1.79	3	–	
43	Isakala-Bamba	Bandundu	Zaire	2	M	–	30.1.79	2	–	
44	Bosokuma	Equateur	Zaire	3	M	–	5.2.79	3	+	Necropsy specimen electron microscopy positive
45	Bosokuma	Equateur	Zaire	9/12	M	–	20.2.79	2	–	Secondary transmission presumed; brother of case 43
46	Bokonzo	Equateur	Zaire	5	M	–	10.9.79	3	–	
47	Olonga (K)	Kasai Oriental	Zaire	1	F	–	30.10.79	3	–	

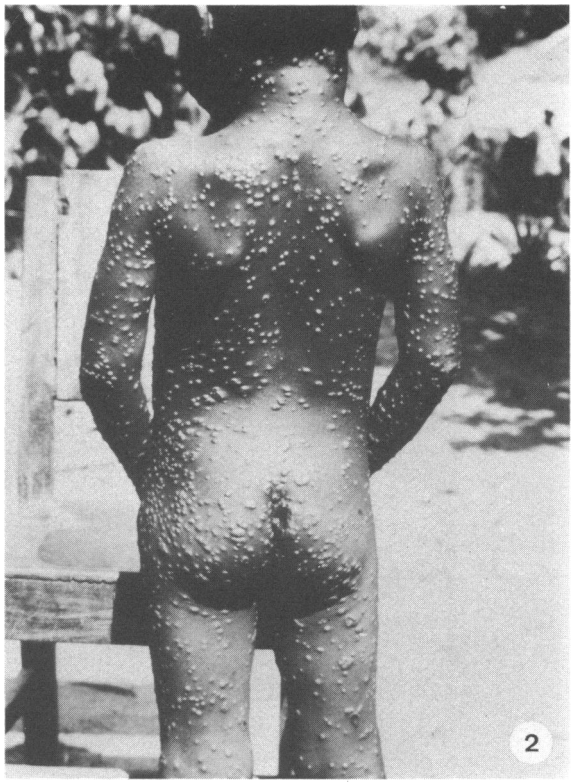
[a] (B) = Bumba Zone; (K) = Kolé Zone.

[b] Severity: 1 = mild (less than 25 lesions with no incapacity, not usually requiring medical care)
2 = moderate (more than 25 lesions, moderate incapacity, usually requiring medical care but not always hospitalized)
3 = severe (more than 100 lesions, severe incapacity, requiring medical care).

Table 2. Virological and serological examinations done on monkeypox cases

Case no.	Virological tests: Days after onset of rash	EM	Virus isolation	Precipitation in gel	Serological tests: Days after onset of rash	Orthopox virus antibodies (reciprocal of titre): HI	CF	Neut.	RIA	Monkeypox virus specific antibody
1	8	NT	+	NT	...					
2	...				13	64	< 8	500		
3	5	+	+	+	90	64	8			
4	...				12	16	< 8	128		
5	8	+	+	–	8	128	16	1024		
6	10	+	+	+	14	160	16	450		
7	6	+	+	+	1518			70		FA +
8	?2	–	–	NT	1509			178		FA +
9	...				44	80	32	16		
					57	40	128	45		
					333	40	8	12		
					1310			29		FA +
10	18	+	+	NT	1383	< 5	⩽ 32			
11	9	+	+	+	...					
12	...				105	40	16	64		
					1663	80	20	450		
13	12	+	–	+	...					
14	10	+	+	+	...					
15	11	+	+	+	30	514	1280			
					1491	80	20	1200	230	RIA +
16	16	+	–	–	18	640		1280		
					1482	80	20	640	400	RIA +
17	8	+	+	+	...					
18	3	+	+	+	...					
19	16	–	+	–	81	40		60		
20	15	+	+	–	100	20		80		
					774	< 5	< 10		365	RIA +
21	6	+	–	–	350	320	20	1200	4700	RIA +
22	16	+	+	+	237	80	10	256		
23	7	+	+	+	63	20	40	90	8200	RIA +
24	7	+	+	+	7	1280	80	< 4		
	13	+	+	+	73	10		570	5900	RIA +
25	9	+	+	–	70	< 5	< 10		740	
26	9	+	+	+	53				3900	RIA +
27	6	+	+	–	50				225	
					50				2300	RIA +
28	15	+	+	+	49	20	40			
29	11	+	–	+	213	160	20		3300	RIA +
30	6	+	+	–	64	40	10	< 10	3000	RIA +
31	15	+	+	+	...					
32	11	+	–	+	48	40	40	120		
33	9	+	+	–	46	80	80	36		
34	5	+	+	+	...					
35	12	+	+	+	...					
36	...				58	20	10		5900	RIA +
					168	10	10		2600	RIA +
37	21	–	–	NT	21	40	20	< 4		
38	5	+	+	NT	15	80	20		483	RIA +
	15	+	+	NT	15	5	10			
					418	10				
39	15	+	+	–	15	160	NT	220		
					30	160	20	32	6300	RIA +
40	...				14	80	40	< 4	7200	RIA +
					302	10				





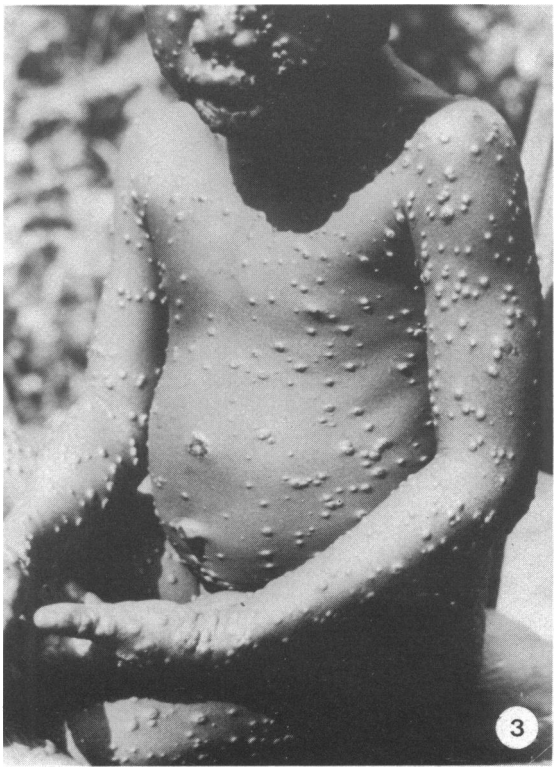


Fig. 1. 7-year-old girl with monkeypox from Equateur Region, Zaire. Front view, during day 8 of rash.

Fig. 2. Same patient as Fig. 1, rear view.

Fig. 3. Same patient as Fig. 1. The old scar on the arm is not due to vaccination.

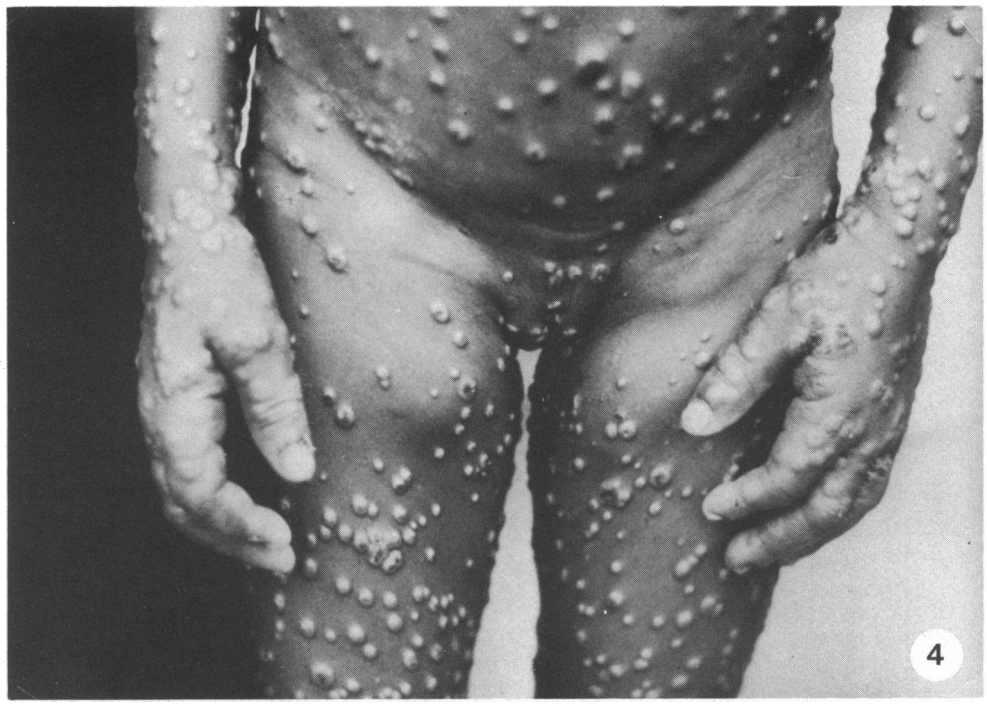


Fig. 4. Heavy concentration of lesions on the hands, inguinal lymphadenopathy, and pustules on genitalia.

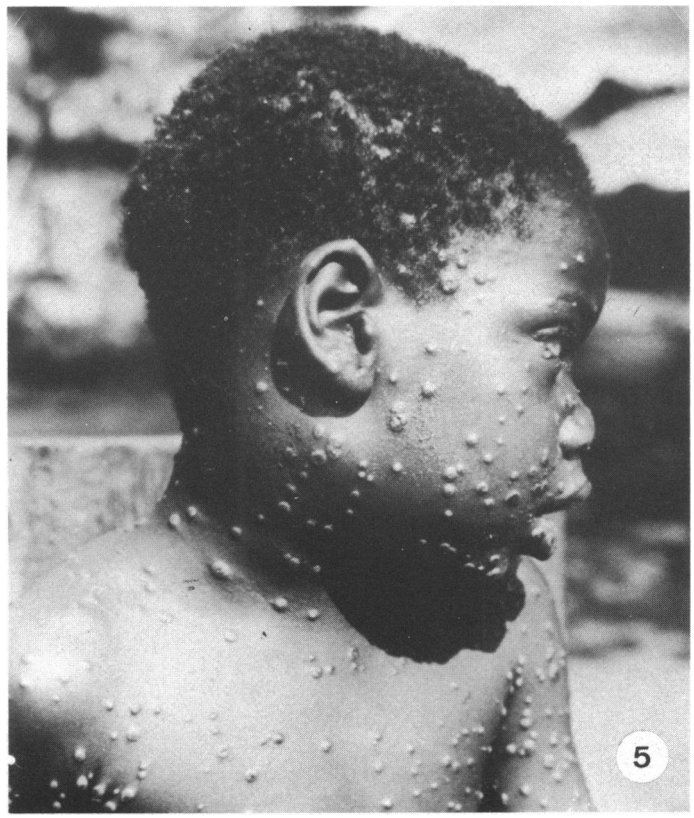


Fig. 5. Swollen lower face and neck due to cervical and submandibular lymphadenopathy.

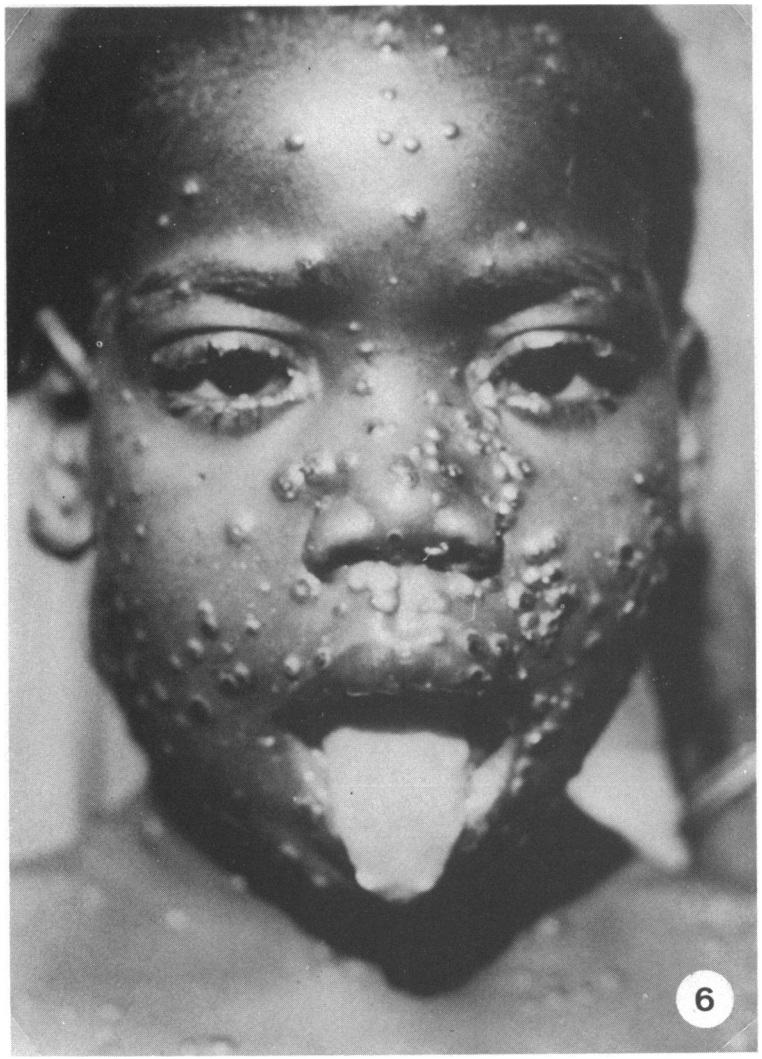


Fig. 6. Lesions on lips, tongue, and eyelid.

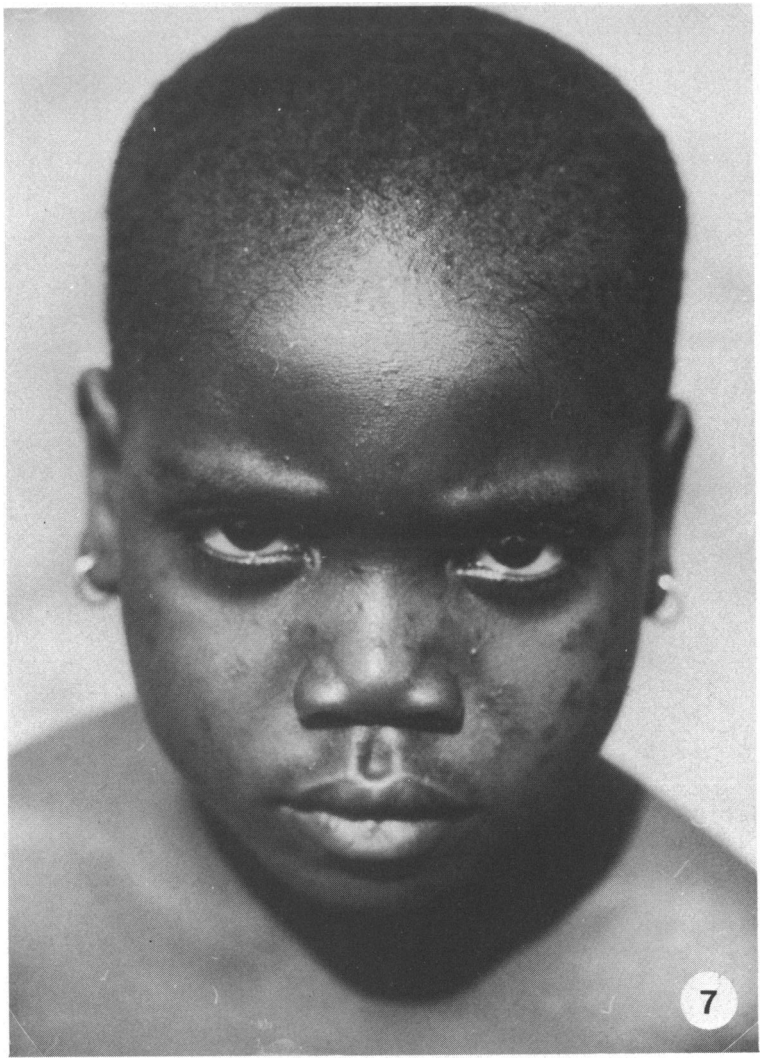


Fig. 7. Same patient as Fig. 6, 16 months after initial illness; hyperpigmentation of lesions with shallow, pitting scars most prominent over bridge of nose.

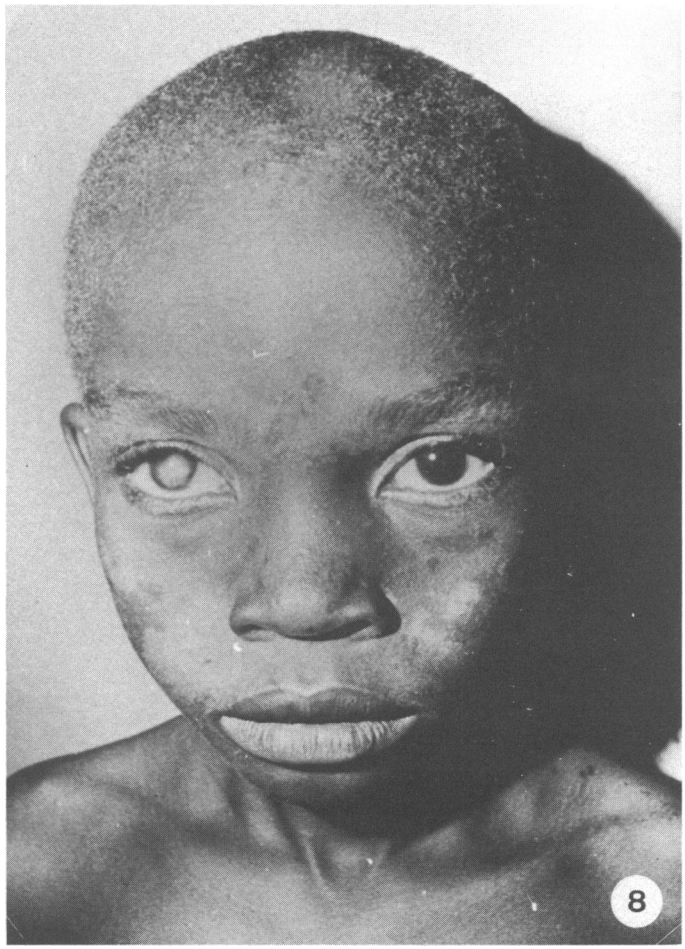


Fig. 8. 8-year-old boy with unilateral blindness following primary lesion on cornea; monkeypox occurred 1 year previously.

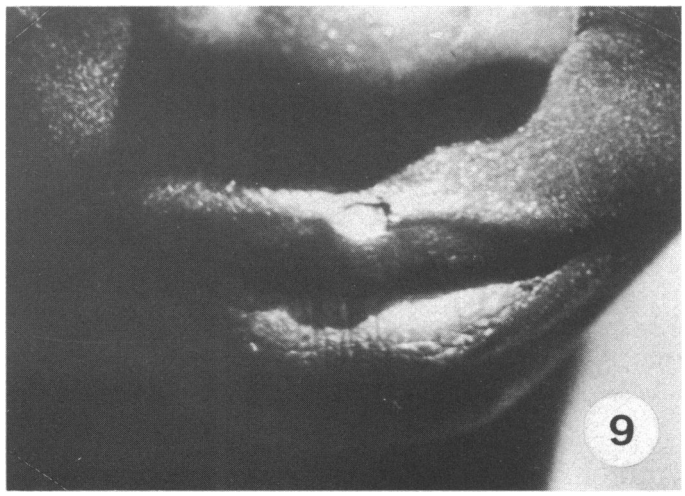


Fig. 9. 0.5-mm pockmark in centre of upper lip in 35-year-old woman who had disease 3 months previously; this was the only lesion on this patient, who had been vaccinated more than 10 years before. Monkeypox virus was grown from the scab taken during the acute illness.

Table 2. Virological and serological examinations done on monkeypox cases (continued)

Case no.	Virological tests: Days after onset of rash	EM	Virus isolation	Precipitation in gel	Serological tests: Days after onset of rash	Orthopox virus antibodies (reciprocal of titre): HI	CF	Neut.	RIA	Monkeypox virus specific antibody
41	4	+	+	NT	91	< 5	< 10	50		
42	6	+	—	—	93	10	10	450	6800	RIA +
	12	+	—	NT	251	20				
43	6[a]				193	40			458	RIA +
44	5	+	NT	NT	...					
45	...				70[b]	31				
46	11	+	+	NT	132	80	10			
47	4	+	+	NT	...					

... = no specimen; EM = electron microscope; HI = haemagglutination-inhibition; CF = complement-fixation; RIA = radioimmunoassay; FA = fluorescent antibody; NT (virological) or blank space (serological) = not tested.

[a] Specimen in formol.

[b] ELISA titre 256.

Serological tests confirmed a previous orthopoxvirus infection in 35 out of 36 patients tested (Table 2). The fluorescent antibody test[b] and radioimmunoassay[c] identified monkeypox antibodies in sera from 19 of the patients. One of these was negative by virological tests, and skin samples could not be collected from 4 others.

In an attempt to detect specific immunological defects, IgG and IgM were determined for 6 patients, using a radioimmunoassay technique. All monkeypox cases had elevated IgG and some were markedly increased; 3 cases had increased IgM. This may reflect only the consequences of the parasitic, bacterial, and viral infections to which these patients had been exposed.

EPIDEMIOLOGY

Geographical and temporal distribution

Cases have been detected in five countries: Zaire (38), Liberia (4), Nigeria (3), Ivory Coast (1), and Sierra Leone (1). One recent case, number 39, originated in Nigeria, but was detected in Benin. All 47 cases have occurred in the tropical rain forest areas of Central and West Africa, between latitudes 8°N and 8°S, where hunting of wild animals for food is common (Fig. 10 and 11). All but 1 of the cases had lived in villages of about 200–1000 persons. The exception (case 18) ate meat originating from the tropical rainforest before disease onset.

Clustering of patients has been observed in countries, in localities within countries, and within families (Fig. 10 and 11). Three of the 4 cases in Liberia (cases 2, 3 and 4) lived in one village, as did 2 of the 3 patients in Nigeria.

In Zaire, 21 (55%) of the 38 cases occurred in the northwestern Equateur region. Within this region, 13 (62%) of the 21 cases have been reported from the Bumba zone, 1 of 21 zones in the Equateur region. Nine cases occurred in the Kasai Oriental region; 8 of these came from the Kolé zone, 1 of 12 zones in this region. Seven cases were detected in Bandudu region and 4 of these were in the Popokabaka zone.

[b] GISPEN, R. ET AL. *Bulletin of the World Health Organization*, **53**: 355-360 (1976).

[c] WALLS, H. H. ET AL. *Bulletin of the World Health Organization*, **58**: 131-138 (1980).

In 5 instances, presumed co-primary cases occurred in the same family (cases 2 and 3, 11 and 12, 26 and 27, 32 and 33, 37 and 38). Case 4 lived next door to one of these families (cases 2 and 3). The interval between onset of illness was less than 24 hours for 1 case, 1 day for 2 cases, 2 days for 1 case, 3 days for 1 case, and 5 days for 1 case; the latter patient (case 38) developed a rash 7 days after the co-primary case (case 37).

The cases have occurred sporadically since August 1970. Six cases were reported in 1970, 3 in 1971, 5 in 1972, 3 in 1973, 1 in 1974, 2 in 1975, 3 in 1976, 6 in 1977, 12 in 1978, and 6 in 1979.

Cases occurred most often in the dry season, although they have been reported throughout the year (Fig. 12). Twenty of the 38 cases in Zaire had onset of rash between January and March.

Age and sex distribution

Children were affected more frequently than adults. The mean age of the patients was 8 years (range 7 months–35 years); the median was 4 years. Thirty-nine of the 47 cases (83%) were below 10 years of age; 25 (55%) were below 5 years, and 5 (11%) were below 1 year. Twenty-six patients were male and 21 were female. However, among patients older than 15 years, 5 of 7 were women.

Person-to-person spread

In 4 families, the onset of rash in secondary cases occurred 9, 12, 15, and 17 days, respectively, after the first case (Table 3). These cases may have been infected from a common source or secondary transmission may have occurred. Three of the 4 index patients had severe disease and the fourth had moderate disease. The disease in secondary cases was milder than in the primary case in two instances and in the other two the secondary cases were of comparable severity. All of the index and secondary cases were unvaccinated. No cases of possible tertiary spread were found.

If it is assumed that all 4 cases represented person-to-person spread of monkeypox, the potential for transmission may be assessed by relating the number of cases to the total

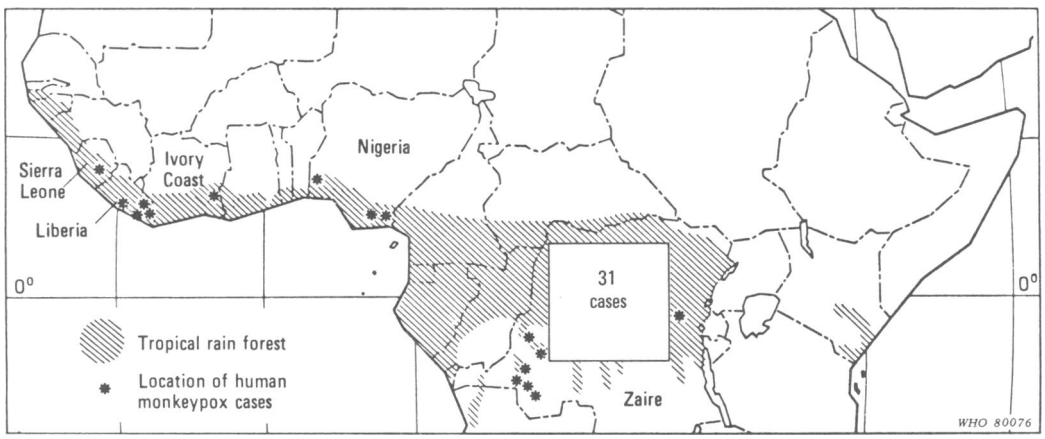


Fig. 10. Distribution of tropical rainforest and 47 human monkeypox cases, 1970-79.

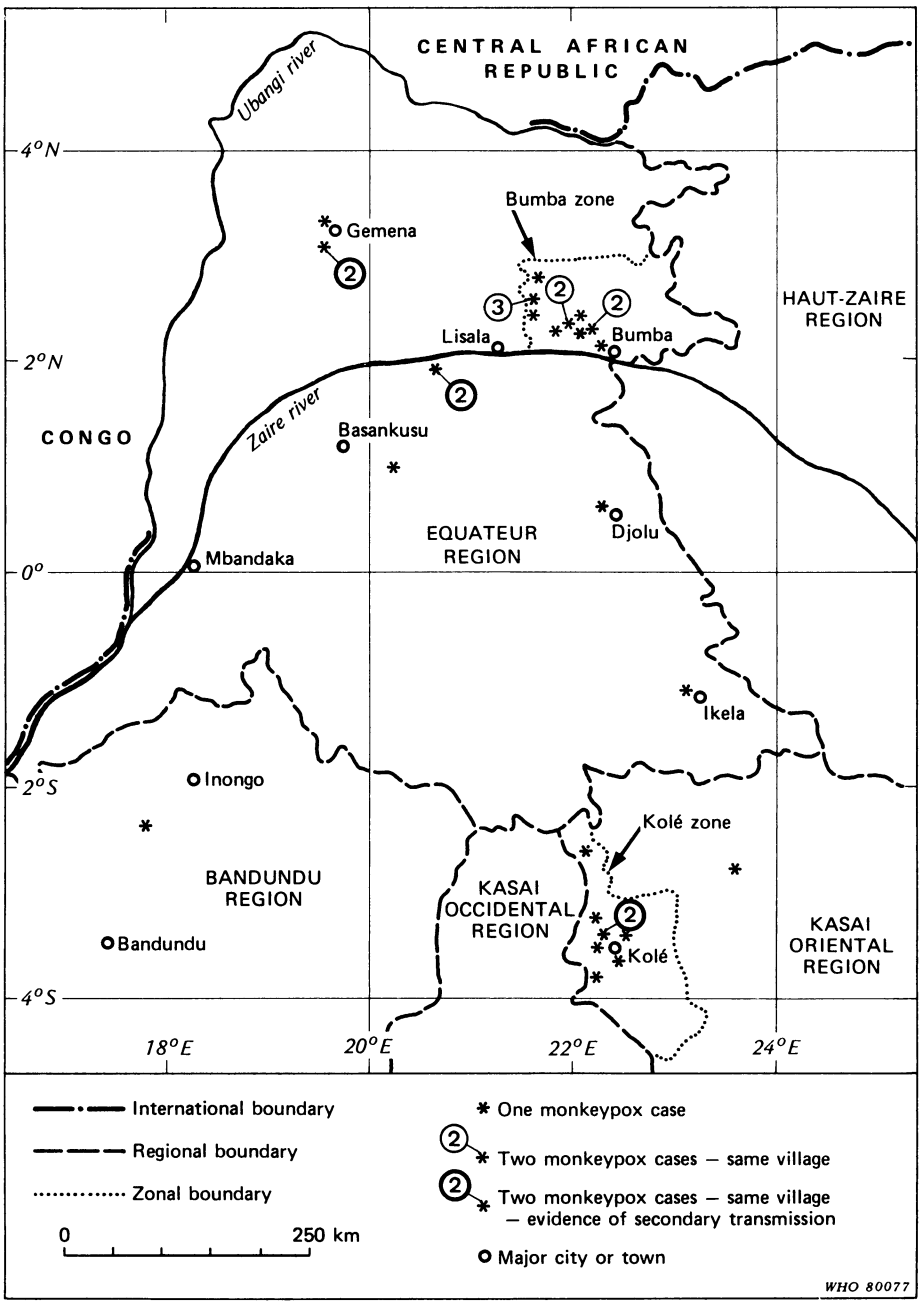


Fig. 11. Distribution of 31 human monkeypox cases in northwestern and central Zaire, 1970-79.

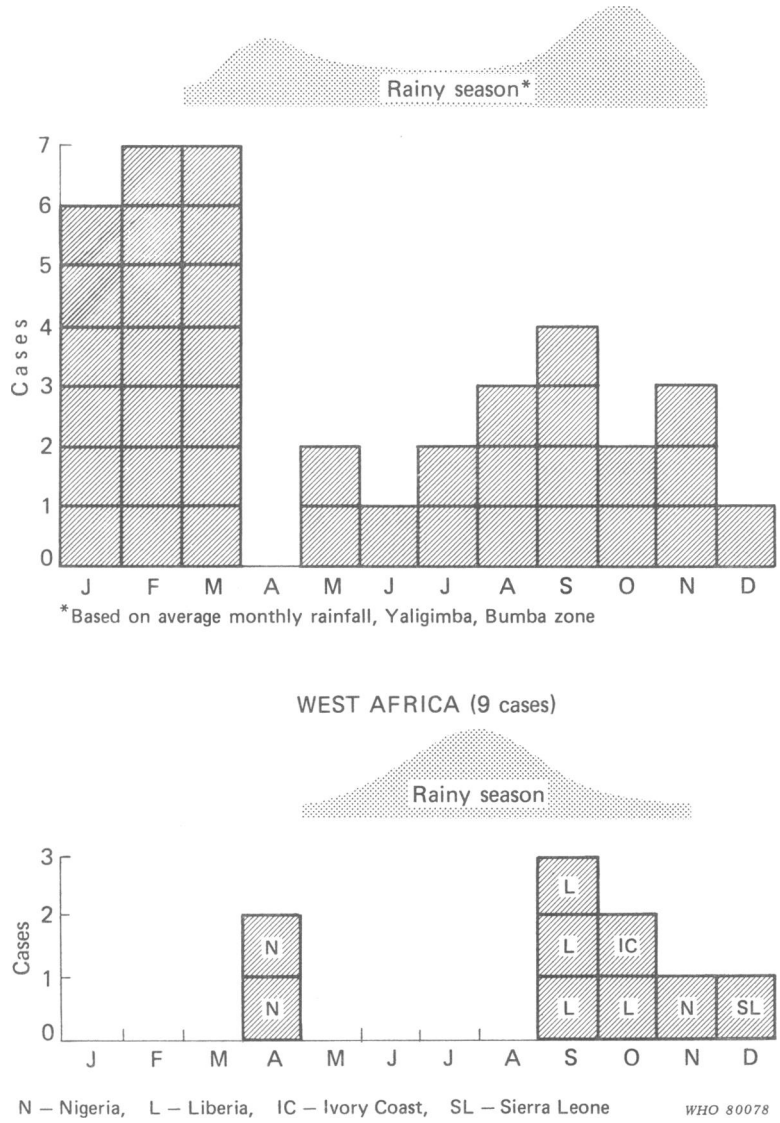


Fig. 12. Seasonal distribution of human monkeypox cases, 1970-79.

Table 3. Pairs of cases of human monkeypox representing possible secondary spread

Case no.	Age	Sex	Relation	Date of onset of rash	Vaccination scar	Severity[a]	Laboratory results[b]								
							Virological			Serological					
							EM	Virus isolation	Precipitation in gel	Days after onset of rash	Orthopoxvirus antibodies (reciprocal of titre) HI	CF	Neut.	RIA	Monkeypox specific antibody
7	4	F	—	9.4.71	—	3	+	+	+	1518	...	...	70	...	FA+
8	24	F	Mother of case 7	18.4.71	—	1	—	—	...	1509	...	...	178	...	FA+
15	3	F	—	10.1.73	—	2	+	+	+	30	514	1280			
										1491	80	20	1200	230	RIA+
16	5	F	Sister of case 15	22.1.73	Doubtful	2	+	—	—	18	640		1280		
										1482	80	20	640	400	RIA+
35	2	M	—	11.9.78	—	3	+	+	+		...	...	...	...	...
36	6	M	Cousin of case 35	28.9.78	—	3	...	...	...	58	20	10	...	5900	RIA+
44	3	M	—	5.2.79	—	3	+	necropsy			...	...	...	...	...
45	9/12	M	Brother of case 43	20.2.79	—	2	...	...	...	70[c]	32	...	...	...	...

[a] 1 = mild (less than 25 lesions with no incapacity, not usually requiring medical care)
2 = moderate (more than 25 lesions, moderate incapacity; usually requiring medical care but not always hospitalized)
3 = severe (more than 100 lesions, severely incapacitated, requiring medical care).

[b] EM = electron microscope; HI = haemagglutination-inhibition; CF = complement-fixation; RIA = radioimmunoassay; FA = fluorescent antibody.

[c] ELISA titre 256.

number of susceptibles (those without a vaccination scar) among family and other close contacts. In this setting the vaccination scar rate among contacts was 70% or more. Among immediate family members (parents, siblings, children, or spouse), the secondary attack rate among susceptibles was 7.5% (3/40) (Table 4); susceptible siblings of monkeypox cases had a 10% attack rate (2/20). Among all other persons having known face-to-face contacts with patients, including more distant relatives, the secondary attack rate among susceptibles was 1.2% (1/83). The total secondary attack rate among all known susceptible contacts was 3.3% (4/123); this is low compared with smallpox where the secondary attack rate is about 25–40%.

Table 4. Vaccination scar rates of contacts of human monkeypox cases, and secondary transmission rates

Contact type	Total no. of contacts	Without vaccination scar		Secondary monkeypox cases	
		No.	%	No.	Attack rate among susceptibles (%)
Immediate family[a]	171	40	23	3	7.5
Other[b]	276	83	30	1	1.2
Total	447	123	28	4	3.3

[a] Parents, siblings, children, or spouse, living in same house during illness.

[b] All other persons, including more distant relatives, having contact with patient during illness, but not necessarily living in same house.

SURVEILLANCE FOR MONKEYPOX

Human

In 1975, special vaccination-scar and facial-pockmark surveys were conducted among populations living near where human monkeypox cases had occurred during the previous 4–5 years in the Ivory Coast, Nigeria, and Sierra Leone. Immunity levels were comparatively low in the younger age groups in these countries and 57% of 2125 children 0–4 years of age, and 29% of 8047 school-age children had no vaccination scars, indicating their probable susceptibility to monkeypox infection. In those areas, there was no evidence of other cases of monkeypox (or smallpox) as determined by surveys of facial pockmarks or by examination of the health units in the area.

From 1975 to 1977, widespread facial pockmark surveys were conducted in Central and West Africa to detect possible cases of smallpox. Over 6 500 000 children of school age and younger were seen; 1 825 380 were of preschool age. None had facial pockmarks suggestive of smallpox or monkeypox, other than the cases known previously.[d]

Data in Table 5 show the results of smallpox vaccination scar surveys done in 1978 and 1979 in villages where cases occurred and in surrounding villages. Less than one-half of the children aged 0–4 years had been vaccinated in villages where cases occurred and about 60% of this age group had been vaccinated in nearby villages. The vaccination coverage in

Table 5. Vaccination scar surveys by age group done near human monkeypox cases, 1978–79

	Village where case occurred						Surrounding villages					
	0–4 years		5–14 years		> 15 years		0–4 years		5–14 years		> 15 years	
Case no.	No.	% vacc.	No.	% vacc.	No.	% vacc.	No.	% vacc.	No.	% vacc.	No.	% vacc.
30	25	88	28	93	64	100	—[a]		—[a]		—[a]	
31	—[b]		—[b]		—[b]		627	81	1126	94	1500	95
32, 33	—[b]		—[b]		—[b]		1212	58	1363	93	2255	97
34	42	50	21	100	47	98	278	69	2296	95	396	93
35, 36[c]	57	7	71	83	119	94	256	34	385	83	513	97
37, 38	112	56	332	95	246	83	—[d]		—[d]		—[d]	
39[e]	205	36	485	53	1897	63	144	45	231	55	569	65
40	118	51	148	78	219	89	2602	66	3883	92	5291	90
41	3	67	20	84	43	99	197	50	362	84	581	99
42	70	37	107	91	131	96	997	52	1537	95	1987	92
43	25	68	6	100	24	100	106	58	155	95	87	99
44, 45[c]	207	46	226	86	421	97	1796	55	2420	89	2288	96
46	161	46	196	83	340	100	—		—		—	
Total	1025	44	1640	77	3551	77	8215	60	13758	91	15467	92

[a] Age breakdown not available; 2558 persons seen, 93% vaccinated.
[b] Combined with data from surrounding villages.
[c] Secondary case.
[d] Included in data for case 40, which was discovered while investigating cases 37 and 38.
[e] Survey done in Omifounfoun, Oyo State, Nigeria; all others done in Zaire.

[d] BREMAN, J. C. (*sic*) *Médécine et maladies infectieuses*, **11**: 550-558 (1978).

the area in Nigeria where case 39 occurred was substantially less than in Zaire. In some areas of the Bumba Zone, over 90% of children less than 15 years old had smallpox vaccination scars as did virtually all adults, as a result of repeated vaccination associated with investigations of monkeypox cases.

During the past 10 years, 1660 specimens have been collected from patients with febrile eruptive disease in Central and West Africa to confirm or rule out smallpox or monkeypox infection (Table 6). Some specimens were collected in preparation for visits of International Commissions to certify freedom from smallpox. Seventy-four per cent of these specimens came from Zaire—the country in which 81% of the cases have been detected—probably because, since 1971, 14 surveillance teams have been in the field in Zaire and a widely publicized reward of about US$ 40 has been given to anybody reporting a confirmed monkeypox case. However, all but 2 of the monkeypox cases were detected and reported by the fixed health units. Two cases were found in Bumba zone by active surveillance in villages near known foci of monkeypox.

Within Zaire there have been differences among regions in specimen collection activities (Table 7). Over 52% of the specimens came from the Equateur and Haut-Zaire regions, but 21 of the 38 cases occurred in Equateur and none in Haut-Zaire. The ratio of monkeypox cases to specimens collected was highest in Kasai Oriental (1 in 8). Roughly 40% of the African tropical rainforest is in Zaire. No cases have been found outside of rainforest areas in Zaire or elsewhere.

Animal

Although cases and outbreaks of monkeypox infection have occurred among nonhuman primates and other animals in laboratories and zoos in Europe and North America, animal

Table 6. Number of specimens received by WHO from selected countries in sub-Saharan Africa, 1970–79[a]

Country	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979
Angola[b]	–	–	–	–	–	–	–	1	99	23
Benin[b]	–	–	–	–	–	–	1	–	1 (1)	6
Burundi	3	–	5	4	3	1	–	–	–	–
Central African Republic[b]	–	–	–	–	–	–	–	–	–	3
Congo[b]	–	–	3	–	–	–	–	2	1	–
Gambia[b]	–	–	–	–	–	–	1	–	–	–
Ghana[b]	–	–	–	–	–	1	–	–	–	–
Ivory Coast[b]	–	1 (1)	–	–	–	9	1	–	–	–
Liberia[b]	4 (4)	–	–	–	–	9	–	–	–	–
Nigeria[b]	–	2 (2)	–	–	–	4	3	–	1	–
Rwanda[b]	10	–	–	2	–	–	–	3	–	–
Senegal[b]	–	–	–	–	–	–	1	–	–	–
Sierra Leone[b]	1 (1)	–	–	–	–	5	3	1	–	1
Uganda	–	–	–	–	–	1	1	–	119	–
Zaire[b]	23 (1)	67	140 (5)	79 (3)	63 (1)	207 (2)	125 (3)	181 (6)	120 (11)	213 (6)
Zambia	–	–	–	–	–	2	–	50	50	–
Total	41 (6)	70 (3)	148 (5)	85 (3)	66 (1)	239 (2)	136 (3)	238 (6)	391 (12)	246 (6)

[a] The numbers of cases of monkeypox are shown in round brackets.

[b] Has tropical rainforest.

Table 7. Specimens received by Ministry of Public Health, Zaire, 1971–79[a]

Region	Estimated population 1974 (millions)	% of total population	No. of medical units (1974)	No. of surveillance units	1971	1972	1973	1974	1975	1976	1977	1978	1979	Total (1971-79)	% of monkeypox cases	% of specimens collected	Ratio of monkeypox cases/specimens collected
Bandundu	3.0	11.8	976	2	11	21 (1)	7	7	14 (1)	4 (1)	15 (1)	38 (2)	6	123 (7)	18	10.1	1/18
Bas Zaire	1.7	6.7	236	1	14	4	3	3	2	3	18	2	—	50	—	4.1	—
Equateur	2.7	10.6	402	2	8 [1]	47 (3)	49 (3)	9 (1)	33	44 (2)	58 (3)	66 (4)	144 (4)	458 [1] (21)[b]	55	36.6	1/22
Haut-Zaire	3.6	14.1	618	2	7	16	8	7	104	21	24	7	8	202	—	16.6	—
Kasai Occidental	2.8	11.0	268	1	49 [2]	15	9	2	8	2	2	3	4	94 [2]	—	7.4	—
Kasai Oriental	2.1	8.3	386	1	11	6 (1)	2	2	6 (1)	2	16 (1)	18 (5)	13 (1)	76 (9)	24	6.2	1/8
Kinshasa	2.4	9.4	120	1	21	7	5	7	11	27	13	5	1	97	—	7.9	—
Kivu	3.9	15.4	645	2	20	9	3	8	6	5	14 (1)	4	4	73 (1)	3	6.0	1/73
Shaba	3.2	12.6	497	2	27	12	3	8	5	—	4	1	4	64	—	5.2	—
Total	25.4	100.0	4148	14	168 [3]	138 (5)	89 (3)	53 (1)	189 (2)	108 (3)	164 (6)	144 (11)	184 (5)	1237[c] [3] (38)[b]	100	100.1	1/34

[a] Some discrepancies with WHO records were noted owing to administrative factors such as the date when the specimens were received, receipt of multiple specimens from some patients, etc. The figures in square brackets give the number of cases of variola, and those in round brackets the number of monkeypox cases.

[b] Includes one monkeypox case detected in 1970; this case is not included in the ratio of monkeypox cases to specimens collected.

[c] Twenty-three specimens taken in 1970 are not included because the breakdown by region is not available.

cases have not been detected in nature; thus the source of human monkeypox infection is still unknown. Epidemiological studies have suggested monkeys and/or rodents as possible sources but, until recently, only a small number of specimens for viral culture had been obtained. Earlier serological studies showed a low prevalence of orthopoxvirus neutralizing antibodies in mammals captured in western and central Africa. In one survey, 10 of 372 sera were positive;[e] 7 were from nonhuman primates (4 chimpanzees from Sierra Leone, 2 monkeys from the Ivory Coast, and 1 monkey from Liberia). Another serological survey failed to detect significant antibodies in over 2000 sera taken from Asian and African nonhuman primates, although none of these animals were known to have come from areas near human monkeypox cases.[f] However, more recent surveys conducted in areas where human monkeypox cases have occurred have shown a 20% (11/55) to 23% (50/215) prevalence of poxvirus neutralizing antibodies in nonhuman primates.[g] In one of these studies antibodies were also found in rodents, other larger mammals, and birds in forest areas of the Ivory Coast and antibodies have also been found in rodents in Zaire. However, only

[e] FOSTER, S. O. *Bulletin of the World Health Organization*, **46**: 569-576 (1972).

[f] ARITA, I. ET AL. *Bulletin of the World Health Organization*, **46**: 625-631 (1972).

[g] MARENNIKOVA, S. S. ET AL. *Voprosy virusologii*, No. 3, pp. 321-326 (1975) (in Russian); BREMAN, J. G. ET AL. *American journal of tropical medicine and hygiene*, **26**: 273-281 (1977); BREMAN, J G. ET AL. *Bulletin of the World Health Organization*, **55**: 605-612 (1977).

recently has it been possible to determine that these antibodies had developed specifically in response to monkeypox virus infection[h] and not to infection caused by any other orthopoxvirus species that might have infected mammals and birds. These, and further refined tests,[i] will serve as valuable tools for epidemiological studies under way in Zaire and others that are still being planned. Special ecological studies began in the Equateur region of Zaire in June 1979 and the results will be reported separately.

Although attempts to isolate monkeypox virus from animals captured near human monkeypox cases have failed, four whitepox virus strains have been identified in organs of animals captured in the wild near such cases. These "wild whitepox" strains came from kidney tissue of one chimpanzee (*Pan troglodytes*), one forest dwelling monkey (*Cercopithecus ascanius*), and two rodents (the sun squirrel, *Heliosciurius rufobrachium*, and the multimammate rat, *Mastomys natalensis*) captured in Zaire.[j] Prior to these isolations two strains of whitepox virus had been previously isolated from routine *Cynomolgus* kidney cell cultures.[k] Whitepox virus cannot be distinguished from variola virus by current biological and chemical methods and, thus, these isolations are of special interest. These findings, however, must be interpreted with caution since the possibility exists that these isolates might represent laboratory cross-contamination rather than primary isolations. Also, it is important to note that existing epidemiological evidence indicates that the virus causing smallpox is not present in Zaire because no human infections with a variola-like virus have occurred there in the period of more than 8 years since the last smallpox case occurred. It can be presumed that the surveillance system is sensitive enough to have detected such cases, since many monkeypox cases have been found.

DISCUSSION

Most cases of human monkeypox have a characteristic clinical appearance, with a 2-day prodrome and typical smallpox-like rash evolving over 2–4 weeks. Severe lymphadenopathy is more prominent among patients with monkeypox than those with smallpox. Six (13%) of 47 cases have been mild or very atypical, suggesting the possibility that unidentified cases may have occurred, especially in areas where surveillance is poor.

While clinical features cannot readily distinguish between smallpox and monkeypox, the epidemiological features are quite distinct. Human monkeypox is a sporadic, infrequent disease detected in small villages in the tropical rainforest of central and western Africa. Only four episodes of possible secondary spread of human monkeypox have been recorded. The 7.5% interhuman transmission rate of monkeypox to susceptible, close family members is much less than that for smallpox. These characteristics, plus the results of serological surveys in animals, indicate that the disease is probably a zoonosis. In addition to these important epidemiological differences, monkeypox and variola virus, both orthopoxviruses, have distinct biological and genetic differences.[l]

The distribution of human monkeypox cases gives only general clues as to the source of this infection. The disease appears to be more frequent in the dry season, as is the case with smallpox. Whether this relates to a possible respiratory mode of transmission, as occurs

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[h] GISPEN, R. ET AL. *Bulletin of the World Health Organization,* **53**: 355-360 (1976); BREMAN, J. G. ET AL. *Bulletin of the World Health Organization,* **55**: 605-612 (1977).

[i] WALLS, H. H. ET AL. *Bulletin of the World Health Organization,* **58**: 131-138 (1980).

[j] MARENNIKOVA, S. S. ET AL. *Bulletin of the World Health Organization,* **46**: 613-620 (1972); MARENNIKOVA, S. S. ET AL. *Acta virologica,* **20**: 80-82 (1976).

[k] MARENNIKOVA, S. S. ET AL. *Voprosy virusologii,* No. 4, pp. 470-473 (1971) (in Russian); GISPEN, R. & BRAND-SAATHOF, B. *Bulletin of the World Health Organization,* **46**: 585-592 (1972).

[l] FENNER, F. *Progress in medical virology,* **23**: 1-21 (1977); ESPOSITO, J. J. ET AL. *Virology,* **89**: 53-66 (1978); MACKETT, M. & ARCHARD, L. C. *Journal of general virology,* **45**: 683-701 (1979).

with smallpox, is unknown. The geographical distribution may represent, in part, an artefact and may be a function of the sensitivity of surveillance and the number of specimens sent for analysis.

Most people in these areas have multiple contacts with a variety of wild animals. All cases have had contact with primates and almost all have had contacts with 2 or more other animals. Young, unvaccinated children and adult females seem to be at special risk; the former, perhaps, because they play with the carcasses of animals after the hunters return to the village and the latter because they are responsible for dressing and cooking the animals and may inoculate themselves during this procedure.

The incubation period of naturally transmitted human monkeypox is unknown, although experiments with monkeys infected by the parenteral route have shown an incubation period of 7–14 days, resembling that of smallpox.[m] Based on evidence from the few cases who had only 1 or 2 animal contacts in the month preceding infection, the incubation time in humans may be about 12 days, similar to that observed in smallpox. Possible "secondary" cases were generally milder and atypical, if indeed they represented inter-human spread rather than primary infection from a common source. When the level of vaccination immunity decreases in Zaire, and elsewhere in West and Central Africa, an increase in cases of human monkeypox may occur, thus providing further information.

Although the natural source of human cases is still obscure, epidemiological and serological surveys suggest that certain animals (forest dwelling monkeys, squirrels, porcupines, or pangolins) may be involved in the natural cycle of transmission. Field studies should focus initially on these animals. Concurrently, serological techniques are being developed which will permit precise measurement of past infection with monkeypox and other orthopoxviruses. This will greatly aid epidemiological investigations of human and animal populations.

The finding of whitepox virus requires that, as for monkeypox, surveillance be maintained and specimens promptly collected and tested if monkeypox/smallpox-like disease occurs in tropical rainforest areas. Laboratory analysis of these and similar strains is necessary for continued confirmation that there is no animal reservoir of variola virus and to monitor orthopoxviruses that might menace man in the future.

ADDENDUM

Monkeypox case 48. A 3-year-old unvaccinated girl from the forest area in the south of the United Republic of Cameroon developed a severe rash on 14 September 1979. Specimens were collected on 30 September. Owing to special problems, monkeypox virus was not isolated from these specimens until January 1980. In February 1980, a complete field investigation was done by a joint team from the Cameroon Ministry of Health, the Organisation de Coordination pour la lutte Contre les Endémies en Afrique Centrale (OCEAC), and WHO. The team confirmed the diagnosis. No other human cases were detected. The child had been in contact with a dead squirrel about two weeks before the illness began. This is the first case of monkeypox reported from this country.

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[m] CHO, C. T. & WENNER, H. A. *Bacteriological reviews*, 37: 1-18 (1973).