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HUMAN MONKEYPOX: UPDATE 1978[1]

by

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1. Introduction

The foundation of the global smallpox eradication programme resides on the assumption that humans are the only natural hosts and vectors of smallpox. Hence, any information which tends to contradict this assumption must be carefully examined. As well, any other agents that cause or might cause smallpox-like illness and smallpox-like transmission are also of great interest to WHO for obvious reasons.

Since 1970, 35 cases of human monkeypox have been detected. The major features of 20 of these cases were reviewed in 1976[1]. The importance of human monkeypox to WHO is that: 1) clinically it resembles smallpox and, therefore, a misinterpretation can be made about worldwide smallpox eradication, 2) the causative agent is an orthopoxvirus, related to but distinguishable from variola virus[2], 3) monkeypox virus strains have been claimed as precursors of "white" clones which have properties similar to "whitepox" viruses, being currently indistinguishable from variola virus[3].

One of the major objectives of this meeting is to examine the monkeypox-whitepox riddle from a biological-research perspective. However, I will review our current knowledge about human monkeypox from an epidemiological view. This will provide a public health orientation, one which is most important to WHO and to countries in and near where monkeypox cases have been reported.

2. Features

2.1 Clinical

The prodrome, eruption and subsequent clinical course of human monkeypox[4,5,6] resembles smallpox, as it was seen in West and Central Africa before eradication[7]. In Table 1 is listed some basic information on the 35 cases. Most (30/35) were classified as having "intermediate" or "severe" illness, presumably indicating that these patients had several days of high fever, widespread abundant lesions and were incapacitated enough to seek medical attention or remain at home without much activity.

Six patients (17%) died; all were less than 7 years of age. Two other children died several months after their illness, from unrelated causes.

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[1] Presented at Informal Consultation on Monkeypox, Whitepox and related Poxviruses, Geneva, 9-10 November 1978.

[2] Medical Officer, Smallpox Eradication Unit, WHO Geneva.

Thirty-one patients had no vaccination scars. The four with scars were 35, 30, 24 and 8 years and had been last vaccinated more than 3 years previously.

2.2 Epidemiological

Where - Twenty-seven cases (1 and 10 through 35) have been detected in Zaire. The others have been found in Liberia (4), Nigeria (2), the Ivory Coast (1) and Sierra Leone (1), all in 1970-1971 (Figure 1).

In Zaire, 14 cases were reported from the northwestern Equateur Region. The Bumba Zone in the Equateur Region had 9 cases.

All but one case occurred in small forest villages of a few hundred persons. These people are mainly hunters and have frequent contact with a wide variety of wild animals. Monkeys are very highly prized as are some of the smaller game. The sole case reported from a large town (Bumba, population 55 000) had recently eaten fresh game bought from a local market near where 2 rodents (Mastomys natalensis, Helioscurius rufobrachium) having the whitepox strains were later captured[1].

When - Between 1 and 6 human monkeypox cases have been reported every year since 1970. All have occurred at least 6 months after the last case of smallpox was detected in the area. Although cases have occurred throughout the year there seems to be a trend to occurrence in the drier months just before the rains. In Zaire, 16 of 27 cases became ill between January and March (Figure 2).

Who - Twenty-eight of the cases have been children 9 years or less. The median age of all cases is 4 years (range, 7 months to 40 years). Eighteen have been male and 17 female. However, 4 of the 5 adults have been female.

Transmission - There has been some clustering of cases. In 4 instances co-primary cases occurred in the same family, as there was a 0-3 day interval between illness onset. One other case lived next door to one of these families and became ill within 24 hours of the others. In two other families second cases became ill 9 and 12 days, respectively, after the first case; thus, secondary transmission possibly occurred but exposure to the same infecting source or to another infecting source, apart from the primary case, cannot be excluded.

The potential for person-to-person spread of human monkeypox has been evaluated using the data from investigations of cases 1 through 34. Family and community members having face-to-face contact with an ill patient were considered susceptible if they had no smallpox vaccination scar (history of smallpox vaccination was felt to be unreliable). Of 56 susceptible contacts only 2, mentioned above, have come down with monkeypox. This 3.6% secondary attack rate is quite low and it is unlikely that the disease would continue to propagate indefinitely in this environment. Transmission to a third generation has not been reported.

Community-wide vaccination scar surveys have indicated relatively low immunity levels in areas where these human monkeypox cases have been reported. Almost 60% of pre-school children in West Africa, living near these cases, had no vaccination scars. There was no evidence of continuing transmission, or of other monkeypox (or smallpox) cases having occurred in these zones 5 years after the initial cases were reported (I. Ladnyi and R. Netter; unpublished data, 1976). Recent investigations in Zaire, likewise, confirm that up to 50% of the pre-school children near monkeypox cases do not have vaccination scars.

Source - The natural cycle of human monkeypox is still unknown. Certain animals (monkeys, porcupine, Gambian rat) have been implicated during field interrogations but monkeypox virus has never been isolated from an animal caught, sacrificed and sampled in Africa. Organs from close to 1000 such animals have been cultured for poxvirus[1]. However, it was during these investigations that the four whitepox strains were identified[8,9].

One interesting study done in West Africa between 1966 and 1970 further indicated the rarity of monkeypox virus in the animal population. Organs from 7 497 different animals were collected in Nigeria and Benin (formerly Dahomey)[10]. Of these, 104 were from non-human primates and over 5 500 from rodents. Eighty-three virus isolates were made but only one poxvirus was found; this was gerbilpox, an orthopoxvirus[11]. In this study organ preparations were injected into suckling mouse brain, a method which may not have been as conducive to poxvirus growth as would use of other culture systems.

Serological surveys have yielded only slightly more information. Over 2 000 samples from African animals have been tested for orthopoxvirus neutralizing antibodies and the results have varied from 0 to 38% positivity[6,12,13]. Wild rodents, antelope, birds and monkeys were found positive in one survey[6]. Monkeypox specific antibody, measured by an indirect immunofluorescent method, has been found in 3 of 4 monkeys captured in areas near where human monkeypox cases were identified[13,14] but this promising test has not yet been widely used.

3. Surveillance

It is difficult to assess the reporting efficiency for human monkeypox detection in West and Central Africa. Firstly, it is puzzling why more cases have not been recently identified in the 4 West African countries with monkeypox cases in 1970 and 1971 and with the last smallpox cases in 1970 or before. These and many other neighbouring countries did widespread surveys from 1975 through 1977 in preparation for certification of smallpox freedom by international commissions. The surveys included the collection of specimens from persons with eruptive disease. No evidence of poxvirus disease in humans was found occurring in this wide area, encompassing 24 countries (except Zaire), after 1971. This, despite the fact that there are many geographic and climatic similarities with the tropical rain forest in Zaire.

In Zaire, the detection of smallpox-like disease has received high priority. Fourteen teams spread throughout the country have been doing smallpox surveillance and evaluation of vaccination activities since 1971 when the last case of smallpox was reported. Zaire teams have sent in over 800 specimens for analysis over the past 6 years. A full time WHO operations officer is working with national authorities to further define the actual incidence of human monkeypox, its inter-human transmissibility and possible source. A $40 US reward is now offered to anyone in the country who reports such a case.

The recent cases in Zaire are now being reported from the centre of the country (Bandundu and Kasai Oriental regions). Whether this represents a change in the natural focus or is an artefact of reporting and specimen collection is to be determined.

A scientific mission to Zaire is planned to attempt to uncover the natural cycle of monkeypox by serological surveys and virologic identification of monkeypox amongst non-human primates and rodents where recent cases have occurred.

4. Conclusions

Human monkeypox probably existed in West and Central Africa before smallpox was eradicated but such cases were thought to be smallpox. Young unvaccinated children seem to be at greatest risk. These children often play with the carcasses of dead animals when hunters return home and drop them in the huts before they are dressed and cooked. Adult females prepare game and may be exposed during this process.

The disease appears to be a relatively infrequent event with little propensity to spread between persons. As such it is problematic if the disease would ever become a major public health problem. Further efforts should be made to better understand the ecology and biology of monkeypox virus. The price paid for smallpox eradication is perpetual vigilance.

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TABLE 1. CASES OF MONKEYPOX INFECTION IN MAN

Case no.	Patient's Name	Village Name	Province	Country	Age (years)	Sex	Vacc. scar	Date onset rash	Severity*	Death	Laboratory				Comments
											EM	Isolation	PIG	Serology**	
1	Lombe	Bokenda	Equateur	Zaire	9/12	M	-	24.8.70	2	-	-	+	-	NA	Died of measles after 2 months
2	Isaac Gweion	Boudua	Grand Geddah	Liberia	4	M	-	12.9.70	2	-	-	-	-	+	
3	Lucretia Tailey[1]	Boudua	" "	"	4	M	-	13.9.70	1	-	+	+	+	+	
4	Monjue Tarlue[2]	Boudua	" "	"	6	F	-	13.9.70	1	-	-	-	-	+	
5	George Grear	Tarr Town	" "	"	9	M	-	2.10.70	2	-	+	+	-	+	
6	Bassie Koroma	Limba Corner	Aguebu	Sierra Leone	24	M	+	1.12.70	2	-	+	+	+	+	
7	Akapego Kann	Ihie Umuduru	Aba	Nigeria	4	F	-	9.4.71	3	-	+	+	+	⊕	
8	Mrs Kann[3]	Ihie Umuduru	"	"	24	F	-	18.4.71	1	-	-	-	-	⊕	Secondary transmission presumed
9	Issouf Yellebeogo	Bosmatché	Abengourou	Ivory Coast	5	M	-	18.10.71	2	-	-	-	-	⊕	
10	Lupaka Lutanga	Ilonga	Kasai Oriental	Zaire	1	M	-	2.3.72	2	-	+	+	-	NA	
11	Migana Madjo	Libela	Equateur	"	3	M	-	27.7.72	3	+	+	+	+	NA	
12	Mbene Ngino[4]	Yamileka	"	"	30	F	+	27.7.72	1	-	-	-	+	+	
13	Bofaso Nsala	Bokokolo	"	"	7/12	F	-	16.9.72	2	+	+	-	-	NA	
14	Ipama Berifude	Niangi	Bandundu	"	2	M	Doubtful	30.10.72	2	+	+	+	+	+	
15	Mopaya Bila	Bogon	Equateur	"	3	F	-	10.1.73	2	-	+	+	+	+	
16	Olonu Bila[5]	Bogon	"	"	5	F	Doubtful	22.1.73	2	-	+	-	-	+	Secondary transmission presumed
17	Elonda Magbanya	Bombana	"	"	7/12	M	-	6.5.73	3	+	+	+	+	NA	
18	Mazongo Ngandi	Bumba Town	"	"	4	F	Doubtful	6.8.74	2	-	+	+	+	NA	
19	Bankeizie Monkanga	Iba	Bandundu	"	40	F	-	4.1.75	3	-	+	+	-	NA	
20	Ishako Okako	Djungula	Kasai Oriental	"	23	F	-	9.3.75	1	-	+	+	-	NA	
21	Iduma Lingai	Ebata	Equateur	"	2	F	-	4.3.76	2	-	+	-	-	+	
22	Mbutu Mambili	Yangomba	"	"	7	M	-	7.6.76	3	-	+	+	+	+	
23	Tsanga Matatuna	Masina	Bandundu	"	8	F	+	27.8.76	3	-	+	+	+	+	
24	Lingoy Asumba	Yamagbe-Bohumbe	Equateur	"	7	F	-	12.2.77	3	-	+	+	NA	+	
25	Monzia Elonga	Yamagbe-Bohumbe	"	"	8/12	M	-	4.3.77	2	-	+	+	NA	+	No contact with case 24
26	Anangi Bomboni[6]	Yamagbe-Bohumbe	"	"	35	F	+	7.3.77	1	-	+	+	NA	+	No contact with case 24
27	Tshikala Esulu	Iwadji	Kole	"	4	M	-	12.2.77	2	-	+	+	-	+	
28	Lubongo Kingengi	Bwalayulu	Bandundu	"	1	M	-	14.3.77	2	-	+	+	+	NA	
29	Nyamuzungu Nyamungama	Katanti	Kivu	"	4	F	-	22.3.77	3	-	+	+	+	NA	
30	Bikaka	Manzita	Bandundu	"	14	M	-	4.1.78	3	-	+	+	-	+	
31	Iyake Lokwa	Ikela	Equateur	"	7	M	-	5.2.78	3	+	+	+	+	NA	
32	Ikopo Ngole	Mongo Senge	Kasai Oriental	"	4	F	-	16.2.78	3	-	+	-	+	NA	
33	Benga Lukfuma[7]	Mongo Senge	" "	"	6	M	Doubtful	18.2.78	2	-	+	+	-	NA	Died of malnutrition after 4 months
34	Ingila Clodine	Imbimbi	Bandundu	"	5	F	-	6.5.78	3	+	+	+	NA	NA	
35	Lukamba Etope	Okela	Kasai Oriental	"	2	M	-	15.8.78	3	-	+	+	NA	NA	

* 1 = mild, 2 = intermediate, 3 = severe

**Positive antibodies to 1 or more of these tests: HI, CF, Neut., RIA; ⊕ positive for monkeypox specific antibody (IF)

[1] Aunt of case 2

[2] In adjacent house to cases 2,3

[3] Mother of case 7

[4] Mother of case 11

[5] Sister of case 15

[6] Mother of case 25

[7] Brother of case 32

FIGURE 1
LOCATION OF 35 HUMAN MONKEYPOX CASES, 1970-1978 (NOVEMBER)

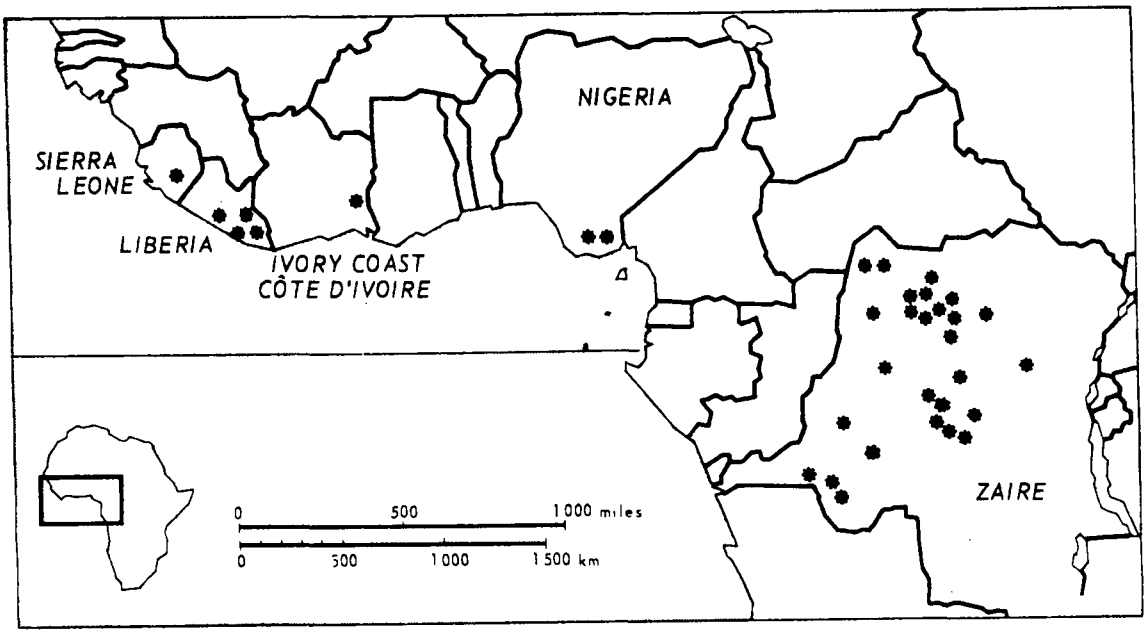
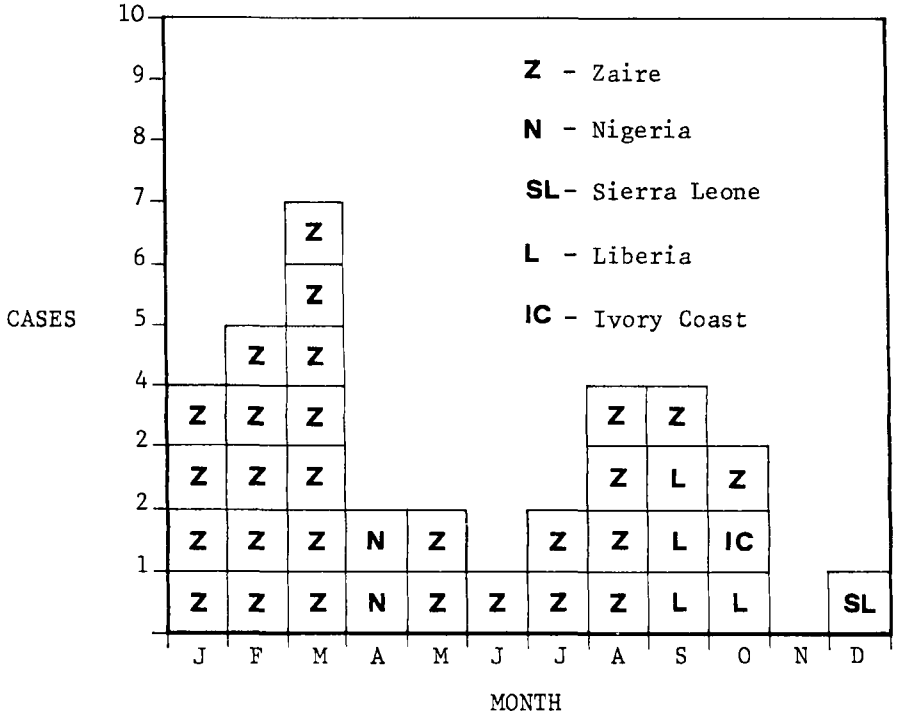


FIGURE 2
DISTRIBUTION OF HUMAN MONKEYPOX CASES BY MONTH OF ONSET



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