Research Recherche

Bulletin of the World Health Organization, 63 (6): 1027-1035 (1985)

Human tanapox in Zaire: clinical and epidemiological observations on cases confirmed by laboratory studies

Z. JEZEK,[1] I. ARITA,[1] M. SZCZENIOWSKI,[2] K. M. PALUKU,[2] KALISA RUTI,[2] & J. H. NAKANO[3]

Human tanapox, a mild disease characterized by a short febrile illness associated with one or more skin lesions, is important because of its possible confusion with smallpox. The article describes clinical and epidemiological features of 264 laboratory-confirmed tanapox cases observed in a geographically limited area in northern Zaire over the period 1979–83.

Tanapox virus, first isolated in 1962, is an unclassified poxvirus (*1*) that produces a mild disease in humans characterized by a short febrile illness associated with one or more localized nodular skin lesions. It was discovered in Kenya, where it caused epidemics in 1957 and 1962 among populations living in flood plains of the river Tana (*2*). The same virus (*3*) was responsible for epizootics among rhesus monkeys in a primate-importing establishment and three research institutes in the USA in 1965-66.[a] Subsequent serological studies in human (*4, 5*) as well as monkey populations (*6*) suggested that tanapox virus is endemic in several countries in equatorial Africa.

Many cases have been seen in Zaire during surveillance activities for human monkeypox, which have been intensified there since 1978. This article reviews clinical and epidemiological features of human tanapox cases observed in a geographically limited area in the north of Zaire during the 5-year period, 1979-83.

MATERIALS AND METHODS

In 1978, an extensive surveillance programme was set up in a specific area in the Mongala subregion in the north of Zaire. For this purpose, a mobile surveillance team based in the town of Lisala searched for human monkeypox and smallpox-like cases and investigated patients suffering from fever followed by skin lesions. At the same time an attempt was made to interview people suspected of having tanapox, to examine them clinically, and to collect material from them for laboratory examination. Most of these people arrived spontaneously to seek medical aid at the team's base; others were discovered when searching for cases of monkeypox. A standard system for making clinical observations, interviews, and specimen collection was introduced from 1979.

Mongala subregion forms part of the Zaire river basin and is covered by tropical rain forest. The economy of the area is based on agriculture, hunting and fishing. The main rainy season is from September to November, with another shorter one in April and May.

The majority of tanapox cases observed occurred in Lisala and in nearby villages located along or near the Zaire river. Lisala, which is the administrative, economic, and educational centre of the subregion, has an estimated population of 70 000, of whom half

[1] Smallpox Eradication Unit, World Health Organization, 1211 Geneva 27, Switzerland. Requests for reprints should be sent to this address.

[2] Monkeypox Surveillance Project, Kinshasa, Zaire.

[3] Centers for Disease Control, Atlanta, GA, USA.

[a] HINMAN, A.R. Epidemic investigation of skin lesions in monkeys and monkey handlers, Special Surveillance Section Report of Epidemiology Branch, Communicable Disease Center, Atlanta, GA, May 31, 1966.

Table 1. Number of tanapox cases examined over the period 1979–83 in the Mongala subregion of Zaire

Year	No. of cases: Confirmed clinically and by laboratory findings	No. of cases: Confirmed clinically	Total
1979	14	25	39
1980	132	35	167
1981	38	17	55
1982	32	7	39
1983	48	9	57
Total	264	93	357

are less than 15 years old. Most of the inhabitants are employed in local light industry, crafts, administrative and educational institutions, or small businesses. The Zaire river has two tributaries that join it near the town; the Kaba river to the east and the Ebabo river to the west. The rivers are used by the population for bathing, swimming, and laundering of clothes. Fishing is traditional among people living along the river banks.

During the 5-year period of observation, 357 persons (180 males and 177 females) showing clinical signs of tanapox were interviewed and examined physically (Table 1). Of these, 306 lived permanently in Lisala while the remaining 51 were from neighbouring localities. The clinical diagnosis was confirmed by laboratory examination (electron microscopy or serology) in 264 (74%) of them, and the present paper is based on these confirmed cases.

Patients were examined physically, interviewed, and skin specimens collected. During the interview attention was paid to patients' movements as well as contacts with diseased humans and animals during the 3 weeks prior to the onset of their illness. In addition, information was collected about exposure to insect bites and time spent by the river or in swamp areas during that period.

Skin specimens including epidermis, necrotic tissue, crusts, scrapings, and smears of exudates, as well as serum samples were collected from patients and sent to the Centers for Disease Control, Atlanta, GA, USA, for laboratory examination. Laboratory test results confirming the clinical diagnosis were the presence of typical poxvirions (enveloped particles or prominent surface tubules) (*7*) identified by electron microscopy. Positive serological diagnoses were based on high titres of tanapox antibodies, detected by neutralization, immunofluorescence, or ELISA.

CLINICAL FEATURES

The clinical features of human tanapox are characteristic and important for establishing the proper diagnosis. In general, the clinical course of the illness has two stages.

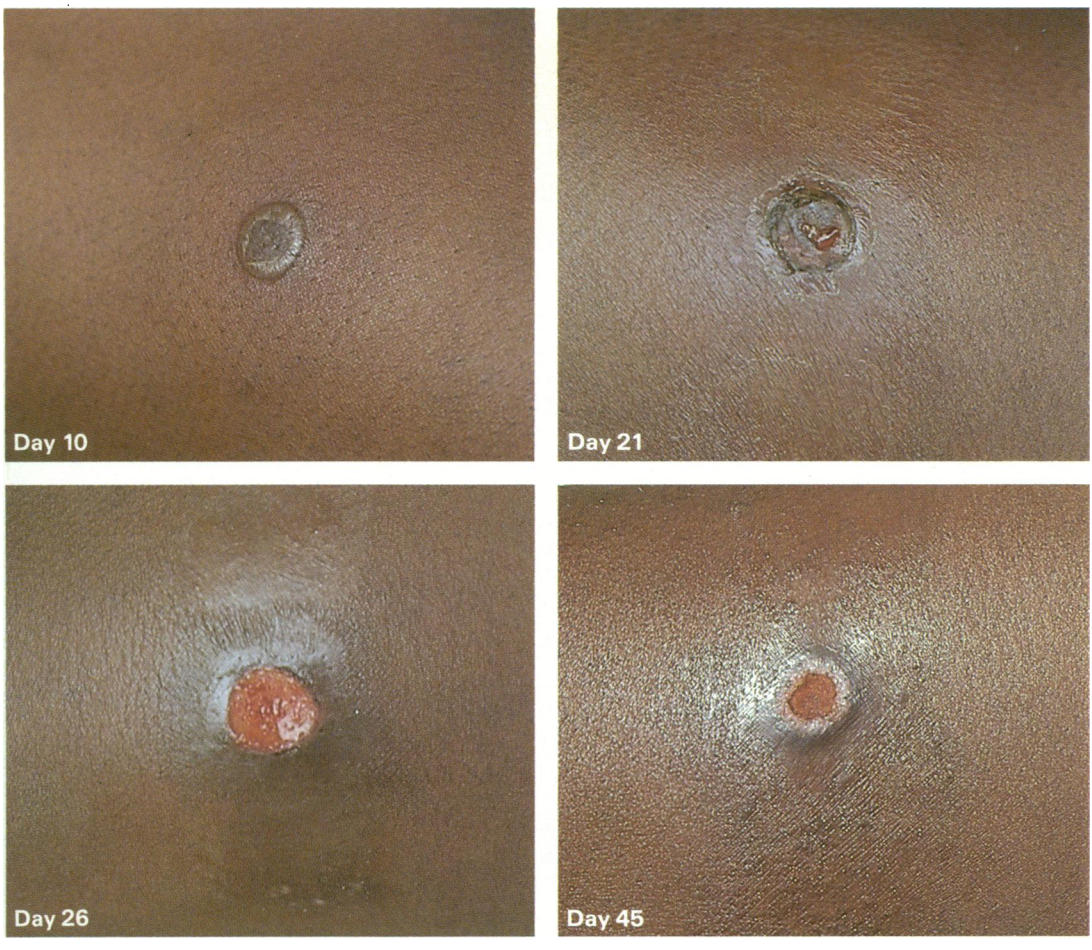
Pre-eruptive stage. In nearly 60% of cases the illness started with clearly manifested pre-eruptive symptoms, the most common being fever, which usually last for 2–4 days. Table 2 summarizes the frequency of fever and the time between its onset and subsequent skin eruption in children, teenagers, and adults in the study. In about 70% of patients, fever started 1–2 days before the skin eruption and in 10% on the same day. When taken, the temperature was usually 38–39 °C and rarely incapacitated the patients. The severity and duration of fever did not correlate with the number of skin lesions.

The short febrile illness was sometimes accompanied by severe headache, backache, and prostration. Headache was the commonest symptom next to fever and in some cases preceded the onset of fever. Opportunities for observing the pre-eruptive stage

Table 2. Frequency of fever and its onset in relation to appearance of skin eruptions among tanapox patients

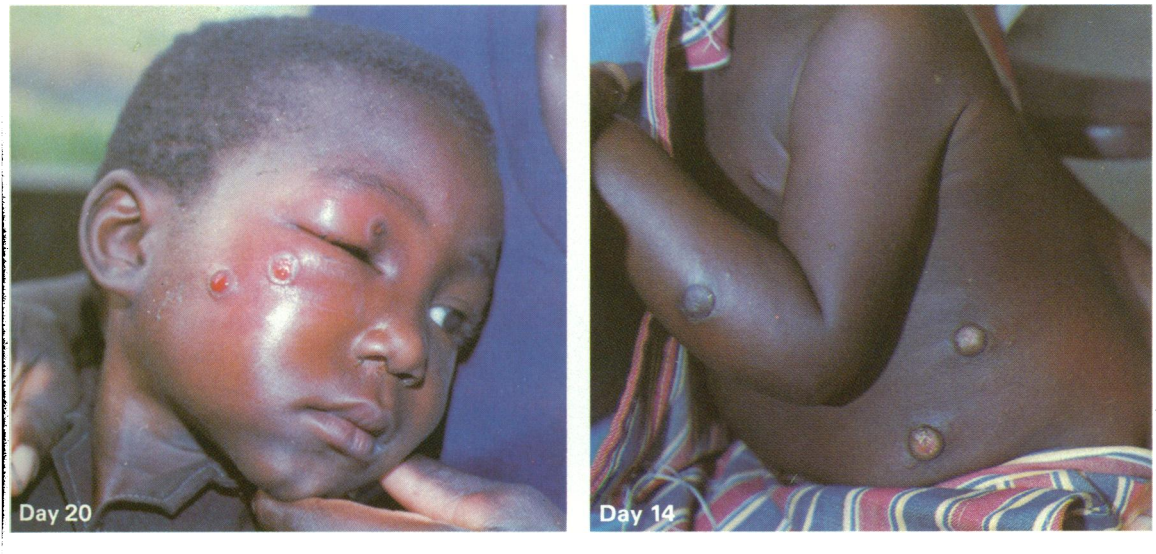
Age group (years)	No. of patients	No. with fever[a]	Period between onset of fever and eruption (days): 0	1	2	3	4
0–9	42	22 (52.4)	2	5	11	3	1
10–19	71	41 (57.7)	4	13	15	7	2
⩾ 20	145	89 (61.4)	9	16	45	15	4
Total	258	152 (58.9)	15	34	71	25	7

[a] Figures in parentheses are percentages.



WHO photo: M. Szczeniowski

Plate 1. Development of tanapox lesions on the 10th, 21st, 26th and 45th days after onset of skin lesion on the right thigh of M.N., a 27-year-old female from Zaire.



WHO photo: B. Otto

Plate 2. Two patients with multiple tanapox lesions.

and the early development of tanapox skin lesions were rare since patients usually sought advice or medical aid only after several days, when the skin lesions had already developed and the corresponding lymph nodes were enlarged. Only 15% of the patients presented within 3 days of appearance of the primary lesion. Sixty-three per cent of the patients sought medical aid within a week of the appearance of the lesion and 30% arrived during the second week complaining of painful lesions and enlarged regional lymph nodes. The remaining 7% presented even later for treatment of ulcers caused by secondary infection.

Evolution of skin lesions. Patients complained of an itching sensation at the site where the lesion eventually appeared, the itching gradually increasing in intensity. The eruptive stage started with the appearance of a circular spot (macule), slightly elevated at the centre but without the central abrasion usually observed in insect bites. The macule, which was readily distinguishable from the surrounding area, became slightly raised and then papular, with a rough surface and a readily palpable underlying induration. The macule was usually darker than the surrounding skin. As the focal skin lesion developed, the fever and general symptoms abated. Concomitantly, the papule continued to grow and developed into an elevated lesion of pock-like appearance that contained little or no liquid but a considerable amount of necrotic tissue. Sometimes the centre became retracted (umbilicated) and on other occasions was covered by a pseudo-crust. Often, especially in lesions located on feet and legs, the rapidly growing papule enlarged into a firm, deep-seated, round, elevated nodule.

By the end of the first week the skin lesion was usually more than 10 mm in diameter with a large erythematous areola several centimetres wide surrounded by swollen oedematous skin (Plate 1, day 10). At this acute stage, local lymphangitis and regional lymphadenitis were common. Regional lymph nodes became enlarged and palpable from about the fourth or fifth day of the onset of the primary lesion and were sensitive to the touch. Lymphadenopathy gradually increased if there was secondary infection of the skin lesions, although neither local gland abcesses nor generalized septicaemia were observed.

In some cases skin lesions developed into large nodules but more frequently broke down as a result of trauma or necrosis and became ulcerated. The ulcers so formed were round, shallow excavations with a lightly raised perimeter and a base formed of soft necrotic tissue. These ulcers spread peripherally as well as into the corium and at this stage of development varied in diameter from several millimetres to 20 mm or more (Plate 1, day 26). Ulcers, especially those on legs and feet, were itchy and sensitive, causing considerable pain and annoyance. Mild fever sometimes reappeared at the end of the second week of illness, but, on the whole, the general effects were much less evident than might be expected from the appearance of the ulceration.

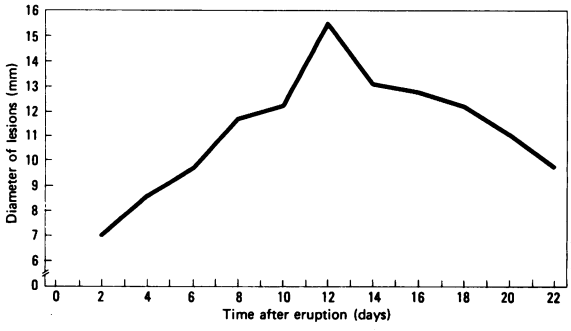


Fig. 1. Average size of skin lesions in tanapox patients following onset of eruptions (feet and legs only).

The average diameter of skin lesions on the lower extremities of the patients observed is shown in Fig. 1 on consecutive days from the onset of the primary skin lesion. On average, the maximum diameter was reached at approximately the end of the second week of illness, but the erythematous areola and local oedema continued to enlarge for a few more days.

After its rapid growth, the ulcer remained about the same size for several days. The acute inflammatory reaction of the surrounding skin diminished and the ulcer's perimeter became flat, and the floor contained granulation tissue. New epithelium formed at the periphery and grew slowly towards the centre of the ulcer, and the regional lymphadenopathy diminished. The healing ulcer was not very painful and did not discharge pus. However, a little semipurulent fluid sometimes formed a scab that disappeared a few days later, to be replaced by a scar whose size and shape were determined by the degree and form of the lesion. The cicatrix was smooth, at first pink and then white, but after a few weeks it became darker than the surrounding skin. Scars persisted but became less noticeable in the course of time.

Location of lesions. In 77% of patients the skin lesions were located on the front of the body; 77% had lesions on the lower part of the body; and 79% were located on parts of the body not usually covered by the clothes, as worn locally.

Only 5% of the patients observed had lesions on the head (i.e., the forehead, the face, and sometimes,

though rarely, the scalp). If lesions occurred on the trunk (7%), they were more often located on the lower back and buttocks than on the chest, waist, abdomen, or axilla and shoulder. The upper limbs were affected in 17% of the patients, usually on the elbow, the lower arm, and the back of the hand; 72% had lesions on the lower extremities, usually on the distal part of the lower legs, ankles, and upper feet. On the distal parts of the legs, lesions were located more frequently on the external side of the limb (63%) than on the internal side (23%), while the remaining 14% were located centrally. Skin lesions were rarely observed on the chest, upper back, waist, axilla, or the soles and heels and were never observed on the neck or lips or in the genital or anal regions.

Multiple lesions. Most patients (78%) had a single skin lesion; in the remaining 22% the number ranged from 2 to 10 (Fig. 2). Multiple lesions (Plate 2) tended to be asymmetrically distributed over the body and were usually in the same stage of evolution but differed in size. Usually the second lesion (and subsequent lesions) occurred within 5 days after the appearance of the first lesion. A generalized rash was never observed.

Prognosis. Human tanapox is generally a benign illness and ulcers or nodules disappear spontaneously within 6 weeks. Although the majority of cases remain ambulant, healing is a relatively slow process. Ulcers that had been incorrectly treated by local remedies, bound with leaves or dirty rags, or located on the feet and exposed to dust persisted for 2 months or more, usually because of secondary infection. However, even severely affected patients recovered without complications and no instances were reported of patients contracting the disease a second time.

Differential diagnosis. In its pre-eruptive stage, the symptoms of tanapox resemble those of almost any other acute febrile illness, and the initial intense itching, together with the appearance of a maculo-papular spot, is usually regarded by patients as scabies or an insect bite. In the later stages of the disease, tanapox patients in equatorial Africa, especially those with multiple lesions, need to be differentiated from patients with human monkeypox. The characteristic features of the skin lesions of tanapox are their slow evolution, solid, nodular form, and large size, together with the absence of pustulation but tendency to ulceration. In cases of monkeypox, skin eruptions evolve relatively rapidly and papules quickly become vesicles and pustules, which can be easily ruptured with an ordinary needle to release a large amount of opalescent fluid. By the end of the first week, all monkeypox lesions are pustular and have attained their maximum diameter of about 5 mm. Tanapox lesions, on the other hand, are prominent, firm nodules that are not easily ruptured with an ordinary needle. Furthermore, they evolve slowly, contain only a small amount of liquid and are full of soft necrotic tissue. The mature lesions are relatively large (diameter > 10 mm) and even those with a pock-like appearance do not pustulate.

Tanapox ulcers are much smaller than tropical ulcers and develop more rapidly. Furthermore, unlike tropical ulcers the surface of tanapox ulcers is not covered with a foul-smelling, grey-green, sometimes bloody slough that forms a membrane attached firmly to the underlying tissue, nor is there the purulent discharge observed with tropical ulcers. No

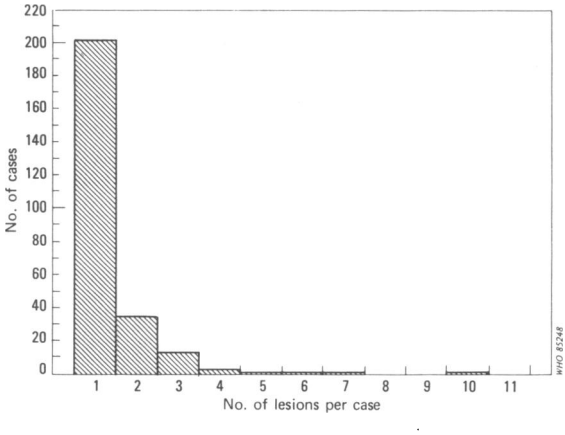


Fig. 2. Distribution of number of tanapox patients according to the number of skin lesions.

Table 3. Age and sex distribution of laboratory-confirmed tanapox patients over the period 1979–83

Age group (years)	Males	Females	Total[a]
0–4	15	8	23 (9)
5–9	12	11	23 (9)
10–14	10	20	30 (11)
15–19	13	28	41 (16)
20–29	42	29	71 (27)
30–39	15	20	35 (13)
40–49	15	8	23 (9)
⩾ 50	12	6	18 (7)
Total	134	130	264

[a] Figures in parentheses are percentages.

relapse of ulceration has been observed at the site of old scars among tanapox patients.

EPIDEMIOLOGICAL FEATURES

The epidemiology of tanapox is poorly understood, but certain important characteristics can be concluded from the available data.

Age, sex, vaccination status, and occupation of patients. Both sexes and all age groups were affected, the majority being adults (Table 3). The mean age of patients was 23.4 years, the youngest being 2 months and the oldest 75 years. Both mode and median were 20 years of age. Only 76 (29%) patients were younger than 15 years of age, which contrasted significantly ($\chi^2 = 7.3$) with distribution of this age group in the local population, nearly 50% of which were below this age, and only 23 (9%) cases were younger than 5 years of age compared with 21% in the local population. The male/female distribution was 51/49 among affected persons, in contrast to that in the local population (47/53).

The majority of tanapox cases had been immunized against smallpox, and only 9% of persons examined had no vaccination scar, being mainly children born after smallpox had been eradicated. Of 236 cases vaccinated against smallpox, 34% developed tanapox within 24 months of primary vaccination or revaccination; 13 persons (5%) developed tanapox within a few months of vaccination, the shortest period being 6 weeks. Altogether, 72% of tanapox cases with a smallpox vaccination scar became ill less than 5 years after successful smallpox vaccination (Table 4). This indicates that smallpox vaccination, which provides protection against orthopoxviruses, offers no protection against tanapox virus.

Table 4. Period elapsed between last smallpox vaccination and onset of illness in tanapox patients

Age group (years)	Total	Period elapsed from last vaccination (years)		
		0–1	2–4	⩾ 5
0–9	27	7	14	6
10–19	67	24	29	14
⩾ 20	142	50	46	46
Total	236	81	89	66

The occupations or main daily activities of the patients varied: 14% were preschool children, the majority of whom often swam and played in the river; 20% were housewives who used to go to the river to collect water, bathe children, wash clothes, and clean utensils; 26% were schoolchildren and students, the majority of whom spent their free time on the banks of the river swimming and fishing: and the remaining 40% were craftsmen, pensioners, and people working

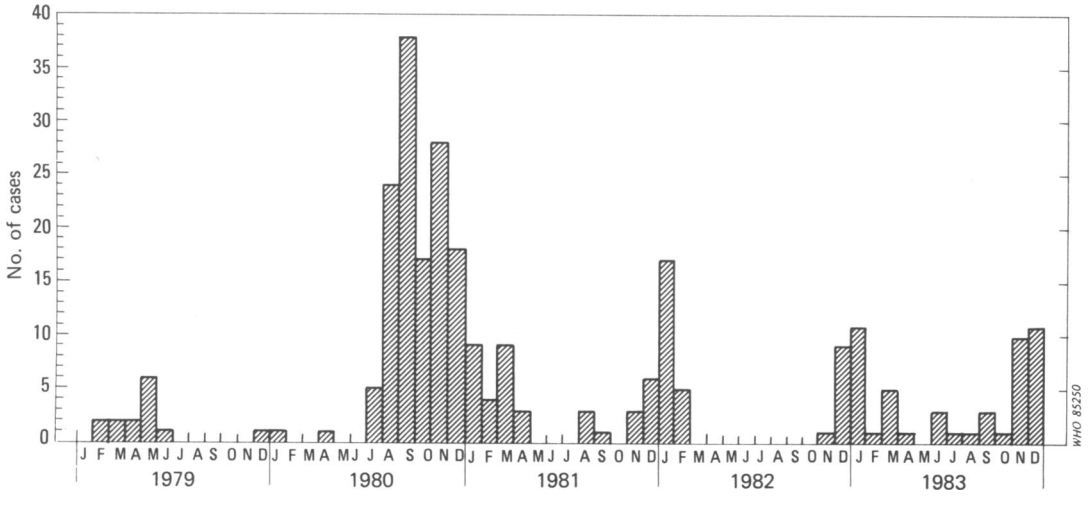


Fig. 3. Distribution of the number of laboratory-confirmed tanapox cases on a monthly basis over the period 1979–83 in Mongala subregion

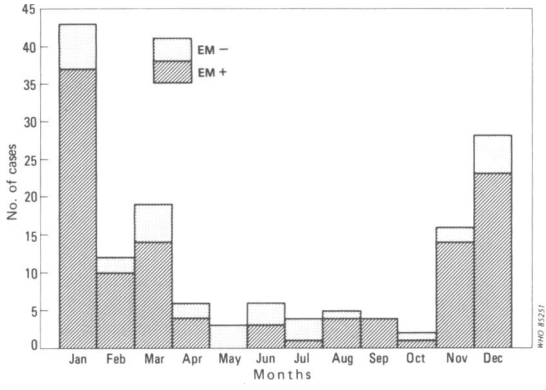


Fig. 4. Seasonal variation in frequency of laboratory-confirmed tanapox cases over the period 1981–83. EM+ and EM− mean positive and negative, respectively, on electron microscopy.

in administration, education, and health services, most of whom frequently spent time by the river. Only nine patients were hunters, traditional farmers, or plantation workers, although these are among the chief occupations in the area.

Temporal and geographical distribution. Over the 5-year period of observation, new tanapox cases were reported each year in the area of observation. The distribution of laboratory-confirmed tanapox cases by month over the whole period, 1979–83, is shown in Fig. 3. The majority of people affected (57%) became ill between July 1980 and March 1981, suggesting the occurrence of irregular long-term changes in disease frequency.

In addition, there seems to be a seasonal variation in the number of cases of tanapox (Fig. 4), cases being more frequent over the 5-month period, November to March.

A clustering of cases in particular locations was also observed. Of 257 cases of tanapox, 57% lived within 300 m of places where similar cases had occurred within the previous 3 weeks: 25% were in the same household and 20% were neighbours of people with tanapox (within about 50 m).

DISCUSSION

Although human tanapox has a benign and nonfatal clinical course, it is important because the causative agent is a poxvirus, and it could be confused with mild monkeypox. In Zaire the geographical distribution of tanapox cases overlaps that of monkeypox. Skin samples, scrapings, or necrotic tissue from lesions sent for laboratory testing without any proper clinical description and resulting in a laboratory report of "poxvirus particles" could cause alarm among public health authorities. Under the electron microscope, tanapox virions are morphologically similar to variola and vaccinia. However, extensive studies of material collected in Zaire indicate that the majority of particles from tanapox patients are envelope-shaped (*7*). Removal of the envelope indicated that the surface tubules were much more pronounced than those usually seen in variola, vaccinia, or monkeypox viruses.

Tanapox does not appear to be a new disease in Zaire. Cases are known to have occurred in the past along large rivers, near swampy areas, and on islands in the Zaire river. Local people called the illness "riverine smallpox" (*nkolokoto ya mayi* in Lingala) or "boutons de Boma" after the town of Boma (at the mouth of the Zaire river several kilometres from the sea) where many such cases are said to have occurred in the past. Besides the cases reported here from Mongala subregion, laboratory-confirmed cases of human tanapox were found in other regions of the country: Equateur, Haut-Zaire, and Kasai Oriental. It is reasonable to expect that this illness also occurs elsewhere, in villages on flood plains or other rivers. However, this benign illness of relatively short duration does not attract the attention of the few medically qualified people in these areas, and cases remain largely unreported.

The incubation period after natural infection is unknown, but when laboratory-passaged viruses were inoculated into rhesus or vervet monkeys or into human volunteers, small papules developed after 3–5 days (*2*).

The mode of transmission among animals and from animals to man is also unknown. The rapid transmission observed among captive monkeys housed together suggested either a common source or constant direct contact between affected and susceptible animals. Animal handlers usually contracted the disease through small scratches on the forearms caused by monkeys (*8*). In Mongala, however, there was no evidence that infection was through direct contact with monkeys or manipulation of their carcasses or that tanapox virus could be transmitted directly from person to person. Tanapox virus was not transmitted when persons with multiple lesions were hospitalized or repeatedly visited the hospital for consultations. Also, there was no evidence that the multiple lesions were caused by inoculation after scratching a primary lesion. Secondary lesions occurred either simultaneously or within 3–4 days of onset of the primary lesion, and they occurred on intact skin, not at the site of skin abrasions. It has been suggested that humans might be infected with tanapox virus from monkeys through arthropods,

possibly culicine mosquitos, by biological or mechanical transmission (*2*). When interviewed, tanapox patients in Mongala revealed that they had been repeatedly bitten by blood-sucking insects, and 79% of tanapox skin lesions occurred on exposed parts of the body. The seasonal increase in incidence of tanapox coincided with the period when mosquitos and other blood-sucking insects were particularly active, but further studies are required.

ACKNOWLEDGEMENTS

We wish to acknowledge the assistance of Lisala surveillance team members and Peace Corps volunteers Miss M. Wernette and Mr B. Otto and to thank the tanapox patients for their cooperation during field work. We also thank Professor Frank Fenner of the Australian National University, Canberra, for advice and for reviewing this article and Mr J. Wickett for his technical assistance in preparing the figures and photographs.

RÉSUMÉ

LE TANAPOX HUMAIN AU ZAÏRE: OBSERVATIONS CLINIQUES ET ÉPIDÉMIOLOGIQUES DE 264 CAS CONFIRMÉS EN LABORATOIRE

Le tanapox humain, maladie bénigne caractérisée par un bref épisode fébrile associé à une ou plusieurs lésions cutanées, est d'un intérêt certain du fait de sa confusion possible avec la variole. Les caractères cliniques et épidémiologiques de 264 cas de tanapox, confirmés après examen de laboratoire et observés dans une zone géographique limitée du nord du Zaïre pendant la période 1979–1983, sont décrits dans cet article.

Chez presque 60% des malades observés, la maladie a débuté par un syndrome pré-éruptif qui comprenait de la fièvre, des céphalées, des rachialgies et de la prostration. Les lésions cutanées étaient formées de vésicules contenant du tissu nécrosé ou de nodules ronds, profondément implantés qui, plus tard, se transformaient en ulcères entourés par une aréole érythémateuse et un œdème local. Une lymphangite et une lymphadénite régionale étaient habituelles. La plupart des malades (78%) ne présentaient qu'une seule lésion cutanée; quand il existait des lésions cutanées multiples (2–10), elles étaient distribuées asymétriquement sur le corps. La majorité d'entre elles (79%) étaient localisées sur les parties découvertes, particulièrement sur les membres inférieurs. La plupart des cas sont restés ambulatoires, et généralement les lésions ont guéri spontanément en cinq à six semaines. En cas d'infection secondaire des ulcères, la cicatrisation a pris plus de deux mois. Aucun malade n'a contracté la maladie une seconde fois.

La maladie touchait les deux sexes et tous les groupes d'âge, encore que la majorité des cas ait été observée chez des adultes. La plupart des malades avaient été vaccinés contre la variole et le tanapox est apparu moins de cinq ans après une vaccination ayant pris, signe que la vaccination contre la variole ne protège pas contre le tanapox.

De nouveaux cas se sont produits chaque année pendant toute la période de l'étude; cependant, suivant la saison et l'année, l'incidence variait considérablement, des cas étant plus fréquemment observés pendant la période où les insectes hématophages sont particulièrement actifs. Un certain regroupement des cas a été observé: 57% d'entre eux vivaient à moins de 300 mètres d'autres cas. La grande majorité des malades passait un temps considérable sur le fleuve, ou à proximité — fleuve qui constitue une aire de reproduction importante pour les moustiques — et ils étaient fréquemment piqués par des insectes hématophages.

Un diagnostic erroné de tanapox est possible aussi bien au laboratoire que sur le terrain. Quand des prélèvements de peau sont examinés en microscopie électronique, on observe des virions dont la morphologie est semblable à ceux de la variole et de la vaccine et des rapports mentionnant la présence de "particules de poxvirus" peuvent alarmer les autorités sanitaires. Si des malades présentant des lésions cutanées multiples, apparues après un épisode fébrile aigu, sont vus sur le terrain ou dans des centres de santé, le diagnostic différentiel avec l'orthopoxvirose simienne de l'homme peut se faire sur la tétrade: évolution lente, forme et dimension des lésions, pas de passage au stade pustules.

REFERENCES

1. MATHEWS, R. E. F., ed., *A critical appraisal of viral taxonomy*, West Palm Beach, CRC Press, 1983.
2. DOWNIE, A. W. ET AL. Tanapox: a new disease caused by a pox virus. *British medical journal*, **1**: 363–368 (1971).
3. DOWNIE, A. W., & ESPANA, C. Comparison of tanapox virus and yaba-like viruses causing epidemic disease in monkeys. *Journal of hygiene*, **70**: 23–32 (1972).
4. MANSON-BAHR, P. E. C. & DOWNIE, A. W. Persistence of tanapox in Tana river valley. *British medical journal*, **2**: 151–153 (1973).
5. AXFORD, J. S. & DOWNIE, A. W. Tanapox. A serological survey of the lower Tana river valley. *Journal of hygiene*, **83**: 273–276 (1979).
6. DOWNIE, A. W. Serological evidence of infection with tana and yaba poxviruses among several species of monkey. *Journal of hygiene*, **72**: 245–250 (1974).
7. NAKANO, J. H. Human poxvirus diseases. In: Lennette, E. H., ed., *Laboratory diagnosis of viral infections*, New York, Marcell Dekker, 1985, pp. 401–424.
8. HALL, A. S. & MCNULTY, W. P. A contagious pox disease in monkeys. *Journal of the American Veterinary Medical Association*, **151**: 833–848 (1967).