Elsevier has created a Monkeypox Information Center in response to the declared public health emergency of international concern, with free information in English on the monkeypox virus. The Monkeypox Information Center is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its monkeypox related research that is available on the Monkeypox Information Center - including this research content - immediately available in publicly funded repositories, with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the Monkeypox Information Center remains active.

development of vaccines against cholera and enterotoxigenic *Escherichia coli*: a review. In: Holme T, Holmgren J, Merson MH, Mollby R, eds. Acute enteric infections in children: new prospectis for treatment and prevention. Amsterdam: Elsevier/North-Holland Biomedical Press, 1981: 443–59.

5 Spira Wm, Saeed YA, Khan UM, et al. Microbiological surveillance of intraneighborhood El Tor cholera transmission in rural Bangladesh. *Bull World Health Organ* 1980; **58:** 731–40.

Food Microbiology Laboratory (T B Morais)**, Department of Microbiology, Immunology, and Parasitology and Department of Pediatrics, Universidade Federal de São Paulo, Escola Paulista de Medicina, São Paulo, Brazil**

Re-emergence of human monkeypox in Zaire in 1996

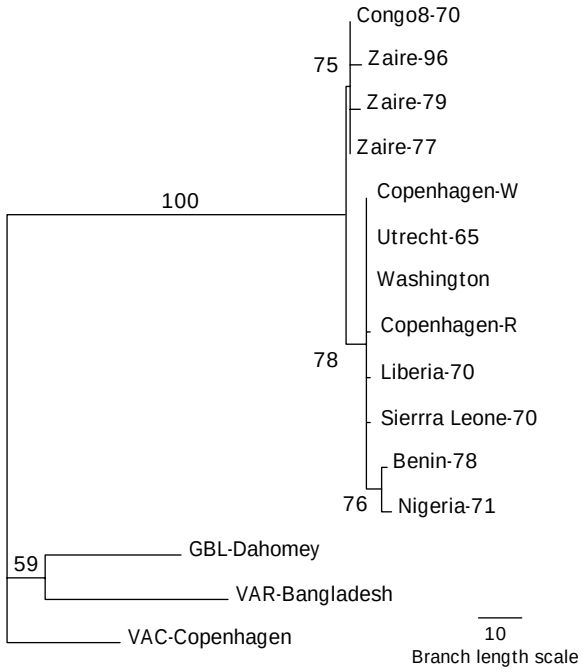
*V B K Mukinda, G Mwema, M Kilundu, D L Heymann, A S Khan, J J Esposito, and other members of the Monkeypox Epidemiologic Working Group**

Human monkeypox is a systemic exanthem, resembling smallpox, that occurs as a sporadic zoonosis in rural rainforest villages of western and central Africa. The disease is caused by an orthopoxvirus, which is transmitted to human beings by handling infected animals; serosurveys have implicated squirrels [*Funisciurus* and *Heliosciurus* spp] as the probable reservoir. Secondary human-to-human spread by aerosol or direct contact accounts for about 28% of cases; tertiary and quaternary chains of transmission are rare.[1]

Between Feb 15, and Aug 31, 1996, 71 cases of human monkeypox, including six deaths, were reported in 13 villages in the Katako-Kombe health zone among a population of 15 698, in Sankuru subregion, Kasai Oriental, Zaire.[2] The outbreak had gone largely unrecognised until the end of July, when an abrupt increase in the number of reported cases led to a preliminary investigation, which found that 42 cases of human monkeypox, including three deaths, had occurred in a small village (population 346) where squirrels were often hunted by men and boys. Most cases were in people under 25 years of age. Among those examined during a preliminary investigation, none had a scar of smallpox vaccination. From February to July, one person in the village appeared to be the primary case-patient who may have been the source of a cascade of human-to-human transmission through eight members of his clan. During this time, monkeypox infections also occurred in other families living together and in a few clans in nearby villages, raising the possibility of other introductions of human monkeypox into the population.

Monkeypox was confirmed in 11 clinically suspect cases from crusted scabs, vesicular fluid, or serum collected from July to September, including three pairs of samples representing secondary contact cases in separate households. Virus-specific polymerase chain reaction (PCR) amplifications of genes for the monkeypox virus haemagglutinin (HA)[3] and tumour necrosis factor receptor (TNFR; unpublished data) were positive for three of four available scab samples, and monkeypox virus was isolated in culture from two of the PCR-positive specimens. In addition, western blot assay showed orthopoxvirus genus-specific IgG in ten different patient sera, and an experimental enzyme-linked-indicator serum assay that used orthopoxvirus antigen peptides showed monkeypox-specific IgM in five of six sera tested.

The present cluster of cases constitutes a reemergence of human monkeypox on a scale greater in magnitude than the approximate 65 annual cases previously indicated for Kasai Oriental, Bandundu, and Equateur regions from 1981 to 1986, and it contains a more extensive occurrence of person-to-person transmission than previously recognised.[1] The extent of the outbreak in Katako-Kombe, which reported no cases during the previous surveillance, and the incidence of disease among household contacts, challenge previous modelling studies[1] that suggested prolonged episodes or sustained cascades of transmission of human monkeypox would be unlikely even after smallpox vaccination, which is protective, ceased. Alternately, the events may represent multiple introductions into the same population because of increasing encroachment of larger populations into the primary habitat of animals in this and other areas of Africa. Because sequence analyses have indicated that Zairian monkeypox strains have not diverged greatly from the first isolate from the area in 1970 (figure) and monkeypox and smallpox variola viruses are independently evolved species,[5] notions of monkeypox virus mutating into variola virus are unfounded.



Phylogenetic analysis of orthopoxvirus TNFR open reading sequences of the current Zairian isolate compared with cognate sequences of monkeypox virus strains from Zaire in previous years and selected non-Zairian monkeypox strains, variola (VAR), gerbilpox (GBL), and vaccinia (VAC) viruses
Nucleotide sequences of genome PCR-generated amplicons were determined using dye-terminated, primer-walking, fluorescence-based Sanger-type reactions[4]. Maximum parsimony analysis of aligned sequences provided bootstrap confidence intervals (values in bold) after 1000 heuristic search replicates weighted for a transition to transversion ratio of 2 (PAUP software version 3·1·1).

In light of the 1996 episode, an international team coordinated by WHO, Centers for Disease Control and Prevention, and the Zairian Ministry of Health began an investigation in February, 1997, to evaluate the outbreak and determine current risk factors for infection. More specific rapid diagnostic assays should enable more precise monitoring of fluctuations in the virus and epidemiological pattern of this zoonosis as changes occur in human demographics, sanitary practices, and reservoir animal distributions.

*Member at Médecins sans Frontières Belgique, Zaire: H Koen. Members at Institut National de Recherche Biomédicale, Kinshasa, Zaire: M Delfi, J J Muyembe-Tamfum. Members at World Health Organization: T F Kweteminga, A Moudi. Members at Centers for Disease Control and Prevention, National Center for Infectious Diseases: L Mangindula, V N Loparev, J M Parsons, D L Jue, T W Crews, J C Knight.

1 Ježek Z, Fenner F. Human monkeypox. Monographs in Virology Vol 17, J L Melnick, ed. Basel, Switzerland: Karger, 1988.
2 WHO. Monkeypox, Zaire. *Wkly Epidemiol Rec* 1996; **71:** 326.
3 Ropp SL, Jin Q, Knight JC, Massung RF, Esposito JJ. PCR strategy for identification and differentiation of smallpox and other orthopoxviruses. *J Clin Microbiol* 1995; **33:** 2069–76.
4 Massung RF, Esposito JJ, Liu LI, et al. Potential virulence determinants in terminal regions of variola smallpox virus genome. *Nature* 1993; **366:** 748–51.
5 Douglass N, Dumbell KR. Independent evolution of monkeypox and variola viruses. *J Virol* 1992; **66:** 7565–67.

Médecins sans Frontières Belgique, Institut National de Recherche Biomédicale, Belgium; Programme Elargi de Vaccination, Kinshasa, Zaire; WHO, Geneva, Switzerland; and Special Pathogens Branch and Collaborating Center for Smallpox and Other Poxvirus Infections, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA (J J Esposito)

Glutathione S-transferase theta 1 (*GSTT1*) gene defect in myelodysplasia and acute myeloid leukaemia

T Basu, R E Gale, S Langabeer, D C Linch

Approximately 30% of cases of myelodysplastic syndrome (MDS) culminate in acute myeloid leukaemia (AML). Ten to 20% of cases of AML have a preceding history of myelodysplasia or evidence of tri-lineage dysplasia at the time of presentation, and this appears to be more frequent in older patients developing AML. Studies of lineage involvement have suggested that whereas AML in younger patients often involves only a single-cell lineage, in older patients a multipotential stem cell is usually involved.[1]

Chen and colleagues[2] have reported that there is a high frequency of the *GSTT1* null genotype in US patients with MDS (46% compared with 16% in a control group). Glutathione S-transferases are involved in the metabolism and detoxification of a range of carcinogens and the above study suggests that MDS might be caused by failure to detoxify such carcinogens, a finding with important implications. We have sought to confirm these findings in UK patients with MDS and AML.

We studied the frequency of the *GSTT1* null genotype in a cohort of 100 young (<40 years) and 100 older (>70 years) patients with AML. These patients were entered into the MRC AML 10 and AML 11 trials and DNA was obtained from the MRC AML trials DNA bank. DNA from 57 patients with MDS and 100 haematologically normal controls (laboratory staff, general medical patients, or women attending the antenatal clinic) was obtained from University College London Hospitals DNA bank. The *GSTT1* null genotype was determined with a PCR-based technique producing a fragment of 480 bp.[3] All cases in which no band was detected were repeated and the integrity of the DNA was shown by amplification of a 250 bp sequence from the β globin gene.

The results (table) indicate that the frequency of the *GSTT1* null genotype is similar in our control group to that previously for a UK population,[4] and there is no difference in the frequency found in either the patients with MDS or AML. The reasons for the difference between the results of the US group and our study are not clear. It is possible that there are major differences in the pathogenesis of MDS in the two countries, although this would be surprising. However, a potential problem in surveys of the frequency of the *GSTT1* null genotype in a given disease is the fact that the frequency of this genotype varies markedly between racial groups, being particularly high in some Asian populations.[5]

Group	Null genotype
Controls	23/100 (23%)
AML: <40 years of age	22/100 (22%)
>70 years of age	21/100 (21%)
MDS	16/57 (28%)

AML=acute myeloid leukaemia, MDS=myelodysplastic syndrome.

Frequency of *GSTT1* genotype in AML, MDS, and controls

Studies purporting to show a difference in genotype frequency in a disease should show that the racial origins of patient and control groups are comparable.

This work was supported by the Leukaemia Research Fund (TB), and Kay Kendall Leukaemia Fund (REG and SL). We thank Sally Pemble for helpful advice.

1 Fialkow PJ, Singer JW, Adamson JW, et al. Acute nonlymphocytic leukaemia: heterogeneity of stem cell origin. *Blood* 1981; **57:** 1068–73.
2 Chen H, Sandler DP, Taylor JA, et al. Increased risk for myelodysplastic syndromes in individuals with glutathione transferase theta 1 (*GSTT1*) gene defect. *Lancet* 1996; **347:** 295–97.
3 Pemble S, Schroeder K, Spencer S, et al. Human glutathione S-transferase theta (GSTT1): cDNA cloning and the characterization of a genetic polymorphism. *Biochemical J* 1994; **300:** 271–76.
4 Warwick A, Sarhanis P, Redman C, et al. Theta class glutathione S-transferase *GSTT1* genoptypes and susceptibility to cervical neoplasia: interactions with *GSTM1*, CYP2D6 and smoking. *Carcinogenesis* 1994; **15:** 2841–45.
5 Nelson H, Wiencke JK, Christiani D, et al. Ethnic differences in the prevalence of the homozygous deletion of glutathione S-transferase theta. *Carcinogenesis* 1995; **16:** 1243–45.

Department of Haematology, University College London Medical School, London WC1E 6HX, UK (D C Linch)

Glutathione S-transferase gene deletions in myelodysplasia

W Atoyebi, R Kusec, C Fidler, T E A Peto, J Boultwood, J S Wainscoat

Chen and colleagues reported on the frequency of null genotypes for the glutathione S-transferases *GSTM1* and *GSTT1* genes showing a significantly increased frequency of the null genotype for the *GSTT1* gene in patients with myelodysplastic syndrome (MDS).[1] These enzymes play a role in the metabolic pathway for carcinogens and it is important for Chen et al's findings to be confirmed. We determined the frequency of the null genotypes in a large group of controls (haematologically normal UK laboratory staff and UK general medical outpatients) and patients with primary MDS. We found no significant difference in frequency between controls and patients for either *GSTM1* (odds ratio 0·89 [95% CI 0·5–1·43]) or *GSTT1* (odds ratio 0·72 [95% CI 0·4–1·34]) null genotype frequency (table). There was no suggestion of any difference in frequencies within the different MDS subgroups. We also looked at eight cases of secondary MDS and found 4/8 to have the *GSTM1* null genotype. The reason for the discrepancy between our findings and those of Chen are not clear.[2] There is the possibility of racial heterogeneity in studies from the USA causing skewed results but other possibilities include, for example, different causes of MDS in different countries.

Group	*GSTM1* null genotype	*GSTT1* null genotype
Controls	54/112 (48%)	18/112 (16%)
RA/RAS	48/97 (49%)	17/97 (17%)
RAEB/RAEBt	22/37 (59%)	11/37 (29%)
CMML	21/32 (65%)	7/32 (22%)
Total MDS	91/166 (55%)	35/166 (21%)

Frequency of *GSTM1* and *GSTT1* genotypes in MDS patients and controls