The late 1970s were a relatively quiescent period in kuru history. The disease’s clinical course (Gajdusek & Zigas 1957; Zigas & Gajdusek 1957; Alpers 1964; Alpers & Rail 1971; Hornabrook 1975), geographical epidemiology (Alpers 1965, 1979) and dissemination by endocannibalism (Mathews et al. 1968) had been well described in the prior two decades. Seminal animal experiments had demonstrated the transmissibility of long-incubating neurological illness (Gajdusek et al. 1966; Gajdusek 1977). Whole cohorts of Fore children born after certain infection-spreading mortuary practices were abandoned in the late 1950s would, for the first time in possibly a century, survive to adulthood without dying of kuru (Hornabrook & King 1975; King 1975). Most tellingly, in each successive year, the median ages of new patients increased by approximately 1 year, a correlation consistent with interdicted transmission. The elusive infective entity appeared less likely to contain DNA or RNA even as molecular genetic techniques for finding nucleic acid improved (Gajdusek 1977; Manuelidis & Manuelidis 1979), but because the Fore no longer faced extermination by kuru, and because community-acquired spongiform encephalopathies were not emerging in other populations except for rare iatrogenic transmissions of Creutzfeldt–Jakob disease, investigative nihilism set into the field of ‘slow agent’ research.

I had an opportunity as a medical student to perform kuru fieldwork for five months in 1979 under the direction of Michael Alpers. I was charged with finding every person living with confirmed or putative kuru in the Eastern Highlands, using Alpers’ guidelines (Alpers 1964). Field assistants Anua Senavaiyo, Auyana Winagaiya and Igana Alesagu from the Papua New Guinea (PNG) Institute of Medical Research (IMR) in Goroka took me to each of the 23 kuru patients known to them in that interval. Our goal was to confirm or refute the epidemiological model that the kuru agent had been transmitted to children of both genders, and to girls and women older than approximately 7 years of age, probably owing to age–gender segregation at mortuary gatherings (figure 1). Each of these 23 patients was born before 1954, again confirming the transmission model. I also refined several family histories of intergenerational kuru, analysed childhood infection cohorts and identified an apparently longer incubation period in boys than in girls (Tarr 1980).

However, my chief effort was to interview the relatives and acquaintances of kuru decedents in the ‘Book’. The Book was the voluminous hard copy line listing of all kuru cases by village from 1957 onwards. Its major contributors in the early years were Patrol Officer Jack Baker (a particularly important contributor), Carleton Gajdusek, Vin Zigas and Alpers, who, in 1970, computerized these data at the NIH. Other contributors included Alex Nilsson, John Mathews, Richard Hornabrook and others from the IMR, kiaps (patrol officers), and many local and visiting doctors, students and missionaries. Steve Ono and Judy Farquhar entered the data from the field into the NIH mainframe computer and generated updated paper copies periodically (figure 2). This systematic collection of the estimated year of birth, symptom onset, death or...
‘recovery’ of every definite, putative or refuted case of kuru (Alpers & Gajdusek 1965) represents ‘shoe leather’ epidemiology in every sense of the term. These data are as unusual as they are important. I know of no other epidemic where every case has been meticulously documented over a half century, or any disease disappearance so thoroughly chronicled. The MRC, to its credit, has supported continued kuru surveillance, analysis and data archiving.

In the late 1970s, the IMR had limited resources to address the many medical disorders in the newly independent PNG. Michael Alpers, who succeeded Richard Hornabrook as IMR Director in 1977, faced these challenges by seeking new funding, expanding malaria, filariasis and nutrition research, founding IMR branches in the Madang and Southern Highlands Provinces, and supporting extensions of Ian Riley's groundbreaking work on lower respiratory tract infection in Huli children and adults in Tari (Riley et al. 1977, 1981; Riley 2002). However, Alpers was one of Gajdusek's original collaborators in Okapa and Bethesda, and his family had maintained part-time residence in Waisa throughout the 1960s and 1970s. Alpers therefore knew the value of kuru surveillance, and how to do it. Most importantly, he recognized that without shouldering personal responsibility for the arduous and underfunded kuru fieldwork, a scientifically precious and unique data collection would meet an untimely end. Michael's telephone call to me in Seattle in 1985 from Goroka (where it was 1 o’clock in the morning at the time) requesting clarification on some field notes I had taken 6 years earlier typified his stewardship of these efforts.

Post-1970s kuru science, well described in this issue of the Transactions, is highlighted by the perseveration of Stan Prusiner in his refinement of small animal models of scrapie (Baringer & Prusiner 1978; Westaway et al. 1987), meticulous chemical methodology (Prusiner 1982; Bockman et al. 1985) and identification of PrP (Basler et al. 1986), and the thorough correlations of John Collinge and his group (Mead et al. 2003; Wadsworth et al. 2004) between host genotype and prion disease expression, thereby explaining the epidemiology of kuru and other human transmissible encephalopathies. However, the people of the Eastern Highlands remain the underappreciated heroes of this saga. Even though not a single one would plausibly benefit from this research, patients and their relatives unfailingly cooperated with kuru investigators for over a half century. Had the people of the kuru-affected region been less tolerant of the repeated and no doubt baffling studies by outsiders, the concept of transmissible, long-incubating, human encephalopathies would have been accepted tardily, if at all, by clinicians, scientists, governments and industry. Such a delay would have further stalled recognition that food of bovine origin could transmit variant Creutzfeldt–Jakob disease (vCJD), and magnified and prolonged the 1990s vCJD epidemic, since so many people in the United Kingdom are at genetic risk because their human prion protein has a methionine at position 129 (Windl et al. 1996). Alpers’ continuity, personality and standards facilitated their cooperation, but in the final analysis it was the enduring altruism of the Fore people and their neighbours in the Eastern Highlands of PNG that enabled knowledge to emerge from the kuru tragedy. Kuru sufferers deserve the gratitude of people worldwide.

Kuru is, or will soon be, extinct (Alpers & Kuru Surveillance Team 2005). The South Fore and their neighbours are not. This story has taught us much about scientific inquiry, and about citizenship.

REFERENCES
Alpers, M. P. 1964 Kuru: a clinical study. Department of Medicine, University of Adelaide.
Alpers, M. P. 1965 Epidemiological changes in kuru, 1957 to 1963. In Slow, latent and temperate virus infections (eds D. C. Gajdusek, C. J. Gibbs Jr & M. P. Alpers). NINDB Monograph No. 2, pp. 65–82. Bethesda, MD: National Institute of Neurological Diseases and Blindness.
Alpers, M. P. 1979 Epidemiology and ecology of kuru. In Slow transmissible diseases of the nervous system, vol. 1, Clinical, epidemiological, genetic and pathological aspects of the spongiform encephalopathies (eds S. B. Prusiner & W. J. Hadlow), pp. 67–90. New York, NY: Academic Press.
Alpers, M. P. & Gajdusek, D. C. 1965 Changing patterns of kuru: epidemiological changes in the period of increasing contact of the Fore people with western civilization. Am. J. Trop. Med. Hyg. 14, 852–879.
Alpers, M. P. & Rail, L. 1971 Kuru and Creutzfeldt–Jakob disease: clinical and aetiological aspects. Proc. Aust. Assoc. Neurol. 8, 7–15.
Alpers, M. P. & Kuru Surveillance Team 2005 The epidemiology of kuru in the period 1987 to 1995. Commun. Dis. Intell. 29, 391–399.

Baringer, J. R. & Prusiner, S. B. 1978 Experimental scrapie in mice: ultrastructural observations. Ann. Neurol. 4, 205–211. (doi:10.1002/ana.410040303)

Basler, K., Oesch, B., Scott, M., Westaway, D., Walchli, M., Groth, D. F., McKinley, M. P., Prusiner, S. B. & Weissmann, C. 1986 Scrapie and cellular PrP isoforms are encoded by the same chromosomal gene. Cell 46, 417–428. (doi:10.1016/0092-8674(86)90662-8)

Bockman, J. M., Kingsbury, D. T., McKinley, M. P., Bendheim, P. E. & Prusiner, S. B. 1985 Creutzfeldt–Jakob disease prion proteins in human brains. N. Engl. J. Med. 312, 73–78.

Gajdusek, D. C. 1977 Unconventional viruses and the origin and disappearance of kuru. Science 197, 943–960. (doi:10.1126/science.142303)

Gajdusek, D. C. & Zigas, V. 1957 Degenerative disease of the central nervous system in New Guinea. The endemic occurrence of ‘kuru’ in the native population. N. Engl. J. Med. 257, 974–978.

Gajdusek, D. C., Gibbs Jr, C. J. & Alpers, M. P. 1966 Experimental transmission of a kuru-like syndrome to chimpanzees. Nature 209, 794–796. (doi:10.1038/209794a0)

Hornabrook, R. W. 1975 Kuru. In Topics on tropical neurology (ed. R. W. Hornabrook), pp. 71–90. Philadelphia, PA: F. A. Davis Company.

Hornabrook, R. W. & King, H. O. M. 1975 Kuru. PNG Med. J. 18, 203–206.

King, H. O. M. 1975 Kuru: epidemiological developments. Lancet 2, 761–763. (doi:10.1016/S0140-6736(75)90737-0)

Manuelidis, E. E. & Manuelidis, L. 1979 Observations on Creutzfeldt–Jakob disease propagated in small rodents. In Slow transmissible diseases of the nervous system, vol. 2, Pathogenesis, immunology, virology and molecular biology of the spongiform encephalopathies (eds S. B. Prusiner & W. J. Hadlow), pp. 147–173. New York, NY: Academic Press. Mathews, J. D., Glasse, R. & Lindenbaum, S. 1968 Kuru and cannibalism. Lancet 2, 449–452. (doi:10.1016/S0140-6736(68)90482-0)

Mead, S. et al. 2003 Balancing selection at the prion protein gene consistent with prehistoric kuru-like epidemics. Science 300, 640–643. (doi:10.1126/science.1083320)

Prusiner, S. B. 1982 Novel proteinaceous infectious particles cause scrapie. Science 216, 136–144. (doi:10.1126/science.6801762)

Riley, I. D. 2002 Pneumonia vaccine trials at Tari. PNG Med. J. 45, 44–50.

Riley, I. D., Tarr, P. I., Andrews, M., Pfeiffer, M., Howard, R., Challands, P. & Jennison, G. 1977 Immunisation with a polyvalent pneumococcal vaccine. Reduction of adult respiratory mortality in a New Guinea highlands community. Lancet 1, 1338–1341. (doi:10.1016/S0140-6736(77)92552-1)

Riley, I. D., Everingham, F. A., Smith, D. E. & Douglas, R. M. 1981 Immunisation with a polyvalent pneumococcal vaccine. Effect of respiratory mortality in children living in the New Guinea highlands. Arch. Dis. Child. 56, 354–357.

Tarr, P. I. 1980 The geography and epidemiology of the disappearance of kuru. Thesis, Yale University School of Medicine.

Wadsworth, J. D. et al. 2004 Human prion protein with valine 129 prevents expression of variant CJD phenotype. Science 306, 1793–1796. (doi:10.1126/science.1103932)

Westaway, D., Goodman, P. A., Mirenda, C. A., McKinley, M. P., Carlson, G. A. & Prusiner, S. B. 1987 Distinct prion proteins in short and long scrapie incubation period mice. Cell 51, 651–662. (doi:10.1002/0092-6747(87)90134-6)

Windl, O. et al. 1996 Genetic basis of Creutzfeldt–Jakob disease in the United Kingdom: a systematic analysis of predisposing mutations and allelic variation in the PRNP gene. Hum. Genet. 98, 259–264. (doi:10.1007/s004390050204)

Zigas, V. & Gajdusek, D. C. 1957 Kuru: clinical study of a new syndrome resembling paralysis agitans in natives of the Eastern Highlands of Australian New Guinea. Med. J. Aust. 44, 745–754.