The Enigma of Slow Viruses

Facts and artefacts, Archives of Virology 6.—*P P Liberski. New York: Springer-Verlag. 1993. Pp 277. DM 250. ISBN 3-2118224278.*

Virology and the law have much in common: a few basic rules like the Ten Commandments and Koch's postulates, and many practitioners who can obscure the basic rules with specialised interpretations. A highly specialised attorney may secure acquittal of a drug dealer caught in the act, despite the Ten Commandments, and a scientist can blame phantom viruses for rare genetic diseases, despite the rules of virology. The latter case is the subject of this book written for the 70th anniversary of Carlton Gajdusek.

Gajdusek won the 1977 Nobel Prize in medicine for the hypothesis that human neurodegenerative diseases such as kuru, Creutzfeldt-Jakob disease, Alzheimer's disease, and scrapie in sheep are caused by "unconventional" slow viruses that "may induce disease months or even decades after infection" (*Science* 1977; **197:** 943–60). This hypothesis has attracted attention because it suggests that kuru is naturally transmitted by cannibalism practised by the Fore tribe in New Guinea; Gajdusek showed that the disease can be experimentally transmitted to chimpanzees by inoculating their brains with homogenates of brains of patients with kuru who died.

But Gajdusek and his followers have not shed much light on this viral hypothesis over the past 20 years. Despite numerous efforts neither the kuru virus nor any other slow virus has been isolated. Therefore, the claim for an infectious origin of these neurological diseases is open to several questions. Why was intracerebral inoculation, instead of feeding, chosen as a model for transmission by cannibalism? Were toxins excluded? —clearly brain homogenates of dead kuru patients must be toxic. Is human kuru indistinguishable from diseases observed in monkeys intracerebrally inoculated with brain homogenates? Moreover, Gajdusek's claim about cannibalism has been questioned because the original photographic documentation that claimed to depict a human was in fact a pig (*Science* 1986; **232:** 1497). Challenged to provide further evidence, Gajdusek cited arrests for cannibalism of New Guineans by Australian authorities (*Science* 1986; **233:** 926).

Despite his admiration for Gajdusek and his fascination with slow viruses, Liberski retains an element of scepticism as the title of his book suggests. It is probably for this reason that he dedicates a lot of space to an hypothesis that offers a "self-replicating" protein (a prion) as a solution to the undetectable enigmatic viruses. The paradox of a self-replicating protein seemed to be solved when the prion proved to be a cellular protein. But that created a new enigma—a pathogenic cellular protein. Prion researchers quickly proposed that mutated prions were to be blamed for neurological disease, until some patients proved to have normal prions and some normal people proved to have mutated prions.

According to this book, conventional and slow viral diseases are about as compatible as night and day. For example, in conventional viral diseases, all viruses contain nucleic acid and can be seen under the electron microscope, whereas in slow diseases, no viral nucleic acid has been found and slow viruses are undetectable under the electron microscope. Conventional viral diseases elicit a febrile response, whereas slow viral diseases do not. Conventional viral diseases, like viruses, spread horizontally, but neurodegenerative diseases such as kuru are "familial", "tribal", or genetically determined, just like conventional genetic diseases. For conventional viral diseases, the latent period between infection and disease is determined by the generation time of viruses (8–48 h) and the number of cells that need to be infected for pathogenicity. For slow viral diseases, the latent period is determined by "incubation period genes" of the host.

In the author's words, the purpose of his book was to summarise "almost all existing data on scrapie and related infections, asking . . . whether [they] fit one complete pattern. Having written this review, the author is convinced . . . that such a task is not possible . . ." However, if one changes one's point of view just a little, a surprisingly complete pattern emerges—the neurodegenerative diseases are conventional genetic diseases and the slow viruses are phantoms of virology. But can we afford an alternative hypothesis in view of the number of papers (more than 1000) on slow viruses that Liberski's book cites? Certainly not until the scientific monarchy of the slow virologists is broken—a process that may be slower than alleged neuropathogenesis by slow viruses.

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