

*Book Review*

## **The Family that couldn't Sleep: Unravelling a Venetian Medical Mystery**

by D T Max

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This book offers fascinating insights into a number of wasting diseases, starting with Fatal Family Insomnia, but going on to mad cow disease, scrapie, and Creutzfeldt-Jakob disease and others. All of these are so-called prion diseases and for anybody teaching in this area the book provides useful examples and background to give to students. The text is wide-ranging from the insomnia in Venice of the book's title, to merino sheep imported into England, to kuru and cannibalism in Papua-New Guinea. At each step the question is raised of what is 'sporadic', what is genetic, and what is infectious?. Along the way we learn about some of the personalities involved including Nobel Prizewinner Staley Prusiner who invented the term *prion* for 'proteinaceous infectious particle'.

Fatal Familial Insomnia (FFI) has been known for at least two centuries in Veneto near Venice. It occurs in a person's 50s, in other words after reproductive age, and so is passed on to offspring. It is autosomal dominant giving a 50% chance of inheriting it compared with a frequency in the general population of about one in 30 million. The inability to sleep (along with other symptoms such as the inability to walk or maintain balance) leads to complete exhaustion and eventually death. The story — really a detective story — about this disease starts the book off, but then further chapters occur interspersed with chapters about other diseases. Much of the book is about prion diseases and the discovery of prions. There is still controversy and Prusiner does not come over as a particularly endearing person. He started work on the diseases (e.g. Creutzfeldt-Jakob) in the 1970s initially thinking that they were caused by 'slow viruses'. However, it could not be shown that nucleic acids were involved while things that destroyed proteins destroyed the infectious agent, and eventually an antibody was obtained making work easier. Nevertheless it is difficult to destroy prions — boiling or heat, radiation, formaldehyde, and other things don't work.

There is an interesting historical story relating to the sheep disease scrapie, dealt with at some length. In the 1740s Robert Bakewell in a village near Leicester aimed to breed bigger sheep by selection to feed the exploding population in the cities. He was successful and the average weight of a sheep went up from 28lb in 1710 to about 80lb by 1795. However, Bakewell was in dispute with Sir Joseph Banks, who bred sheep for wool rather than their meat, there were problems with scrapie. Merino sheep were imported secretly from Spain to improve the breed, but by 1820 scrapie was threatening to destroy the mutton and wool industries. The story is given in detail but by 1913 Australia had taken over sheep production and scrapie had all but disappeared: it was referred to in publications as "an obscure disease of sheep".

Another large section of the book deals with Creutzfeldt-Jakob disease and kuru from Papua New Guinea. A German doctor, Hans Creutzfeld, had diagnosed a patient in 1910 with a fatal degenerative disease and at autopsy the patient's brain showed 'dead neurons'. The condition was picked up later in several patients by another German neurologist, A. M. Jakob, hence the name. Kuru was a similar disease identified in Papua-New Guinea and there is a fascinating story told here about Carleton Gajdusek's investigations in that country (as well as his sexual proclivities for which he was briefly jailed in 1997).

The prion hypothesis continued to gain ground, and between 1975 and 1997 Prusiner had been awarded about \$56 million in grants to investigate the phenomenon. However, a British mathematician, J S Griffith, at Bedford College in London had suggested that a protein could somehow convert another protein from one form into another potentially damaging form, although this did not receive much attention at the time possibly because he was a mathematician. This may indeed be how prions work — but there is a whole lot still to be discovered.

Another story described in the book is that of the recent Mad Cow Disease, or Bovine Spongiform Encephalopathy (BSE), which produced an epidemic in British cattle, and resulted in the slaughter of over 3 million older animals in the UK. The hotly debated question was whether this could be transmitted to humans to produce “variant CJD”, and whether we were to expect an epidemic in humans. So far about 150 British individuals have died of vCJD — but it remains to be seen whether there is more to come! As one scientist said, “we don’t know if we are out of the wood yet”. The final section of the book delves into treatments for the ‘incurable’ CJD, and especially the use of a material called pentosan. It is not clear whether this actually works but there is a problem that pentosan is too large to penetrate the blood-brain barrier, and so it has to be injected into the brain. Few surgeons are prepared to do this.

The poignant ending to the book comes when the author finally reveals that he has a non-fatal, non-prion, slowly progressive neuromuscular disease, a variant of Charcot-Marie-Tooth disease, which is due to a mutation. He has interviewed a long list of scientists about prion diseases, including Stanley Prusiner (he says ‘fitfully’), and has read extremely widely (there is an extensive list of *Sources* at the back as well as an Index).

This book gives us history, medicine, genetics, as well as molecular biology, in a very readable form. It would be understandable to the layperson or by the young student or schoolchild, but to scientists (and medical people) it will perhaps resound more strongly. This is not just because of the science and the medical progress, but also because of the accounts of the personalities and the twists and turns that scientific discovery takes, as well as the controversies that continue in this area. There are no graphs, diagrams or photographs to put off the non-scientist. The book is highly readable and highly recommended.

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