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In this month's free article on pages 809–819, Claudio Soto reviews a subject that, in our opinion, is often neglected — how to diagnose prion diseases.

The prion diseases, also known as transmissible spongiform encephalopathies (TSEs), are fast-progressing degenerative neurological disorders that include Creutzfeldt–Jacob disease (CJD) in humans. In the UK, CJD is often referred to in the press as 'the human form of mad cow disease', in light of the connection between a new form of the disease, variant CJD (vCJD), and the consumption of BSE-infected meat products.

As Soto describes, the nature of prion diseases is not only an interesting conundrum from a scientific research point of view, it also presents unique difficulties in terms of infection diagnosis. The protein-only nature of the infectious agent precludes the use of nucleic acid-based PCR, a technique now widely used in the diagnosis of other infections. Additionally, the diagnosis cannot be based on the immune response because the causative agent is an altered form of a normal cellular protein and infected individuals therefore do not mount an immune response.

Yet the development of a non-invasive, early pre-mortem diagnostic test, and even a pre-symptomatic test, is highly desirable, particularly in light of the recent publication of details of a second UK case of human-to-human transmission of the disease via infected blood products, which is highlighted in our Disease Watch News this month. The best option for a non-invasive test seems to be a blood-based assay, but much work remains to be done, as Professor Soto estimates that the current tests require an increase in sensitivity of 2–4 orders of magnitude.



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