Safe laboratory management of prions and proteopathic seeds

Prions, the infectious agents of fatal and transmissible neurodegenerative disorders in humans and animals, are comprised of assemblies of misfolded forms of prion protein (PrP). The death of a 33-year-old researcher of prion diseases from variant Creutzfeldt-Jakob disease (ie, the strain of disease that is derived from bovine spongiform encephalopathy) 9 years after a percutaneous exposure to prion-contaminated material, and the death from or diagnosis of prion disease in two other people in Europe after working in prion research, emphasises the importance of statutory guidance for laboratory safety when working with dangerous pathogens.[1] People in numerous laboratories handling diagnostic blood, CSF, and other low-risk biofluid samples from patients with or suspected to have Creutzfeldt-Jakob disease have contacted us to suggest that the existing guidance was not sufficiently clear or proportionate.

Evidence has accrued for the potential for proteins that are linked to neurodegenerative diseases, other than PrP, to adopt abnormal conformations, self-propagate, and cause transmissible pathologies and diseases in humans and laboratory animals.[2,3] These proteins share a range of pathological properties but are also distinct from prions in important ways, including that there are no known animal or human epidemics or established occupational risks. Experiments that involve inoculating, concentrating, or synthesising these so-called proteopathic seeds have become routine in the past decade, but no statutory guidance is available for safety. Human–human transmission of amyloid β proteopathic seeds has been observed in some specific circumstances that were also shown to transmit prion infection (eg, use of cadaver-derived human pituitary hormones or dura mater in neurosurgery) and can cause iatrogenic cerebral amyloid angiopathy and fatal brain haemorrhage after long latencies.[4] The popularity of this field of research, and the long latencies that are to be expected for diseases that are caused by these proteopathic seeds, mean that occupational exposures might not yet have resulted in any clinical consequences. It is prudent, therefore, to consider potential risks from laboratory work involving these agents.

The UK's Advisory Committee for Dangerous Pathogens convened a subgroup to revise guidance for safe working with prions and to consider whether any measures were needed for work with proteopathic seeds, involving experts from research laboratories for prion and other neurodegenerative diseases, infectious disease specialists, pathologists, veterinarians, and health and safety experts. In the new guidance, we emphasise a distinction between high-risk CNS tissues and research samples that contain high concentrations of prions, which need to be managed in specialised laboratories with strict policies, and low-risk biofluids, such as blood and CSF, from patients who are suspected to have Creutzfeldt-Jakob disease with no or low concentrations of prions, which can be managed in a high-throughput diagnostic laboratory setting through adherence to appropriate general laboratory practices.

We also concluded that the poorly defined pathogenicity in humans of proteopathic seeds when prepared in concentrated forms for biochemical, structural, or transmission studies means that they should now be considered as hazard group 2 pathogens, necessitating work in a containment level 2 facility. We recommend a range of safety measures,[5] including special attention to risk assessment and staff training; recording of accidental exposures; special caution with the use of any sharp tools to avoid percutaneous injury; work inside a microbiological safety cabinet; and the use of spill trays, absorbent material, and defined procedures to decontaminate equipment and spills to avoid contamination of the laboratory environment.

Importantly, we do not recommend any changes to existing procedures for the routine handling of tissues and biofluids from patients with non-prion neurodegenerative conditions for diagnostic or research purposes. We hope that this new guidance will be seen as proportionate and precautionary and help organisations to have increased confidence about the safety of their employees.[5]

We declare no competing interests. Members of the Advisory Committee for Dangerous Pathogens Transmissible Spongiform Encephalopathy Subgroup are listed in the appendix.

See **Online** for appendix

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