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Commentary

Instrument cleanliness and protein misfolding disorders

The percentage protein composition of human tissue varies from some 8% in plasma to around 20% in liver, and hydrophobic proteins or those with many exposed -SH groups are more difficult to remove from surfaces, particularly stainless steel. The abnormal forms of the prion protein (PrPSc), responsible for causing spongiform encephalopathies, including Creutzfeldt–Jakob disease (CJD), are largely composed of beta sheets that form strongly hydrophobic aggregates which, once in contact with and dried on surgical instruments, will no longer dissolve in water or many commonly used detergents [1]. There are case reports of transmission of CJD via neurosurgical instruments, dating back to the 1970s [2], and a number of case–control studies, admittedly equivocal but hardly reassuring, have identified assorted surgical operations as risk factors for disease [3], most notably the studies that used, as their sampling frame, the particularly complete national disease registers in Denmark and Sweden [4]. Thus the widespread exposure of the UK population to beef potentially contaminated with the agent of bovine spongiform encephalopathy (BSE) in the 1980s and 1990s and the demonstration that this was likely to be the cause of variant CJD (vCJD) in humans [5] gave rise to a number of initiatives to ensure that the cleanliness of surgical instruments would be such as to prevent further sustained spread of these diseases as a result of surgery.

In this context, the paper by Smith *et al.*, published in this journal last year [6], represents encouraging news. It suggests that proprietary National Health Service plastic bags and sterile-water-soaked wound pads were equivalent in efficacy to commercial precleaning and significantly less expensive. *En route* to this conclusion, the authors also discuss the upper levels of residual protein variously being recommended as well as the two different ways of assaying residual protein: sodium dodecyl sulphate (SDS) extraction and assay of eluent using orthophthalaldehyde (OPA) solution vs analysis *in situ* using OPA. Current guidance in the UK [7] recommends, alongside various improvements in the whole cleaning and decontamination process, that the upper limit of residual protein should be 5 μg per instrument side (less for neurosurgical instruments), and that elution and swabbing techniques to estimate residual protein should not be relied upon [8]. To consider the latter recommendation, first, this was based on the demonstrably adherent properties of prions which implies that protein measured in any eluent may not reflect the protein that remains on the surgical instrument. This has been questioned [9,10] but, nevertheless, most generally agree that *in situ* measurement techniques are the safest option for instruments to be used on tissues at high risk of transmitting disease such as brain and spinal cord, even if elution and swabbing techniques might have a place for instruments used on other tissues. Ultimately, resolving this question would require a comparison of techniques using tissue containing PrPSc that would either show, or not, a consistent relationship between the protein measured on elution and that remaining on the instrument. The 5 μg or less per instrument side represents a more exacting standard than the 6.4 $\mu g/cm^2$ currently being proposed by the International Organization for Standardization (ISO). The UK figure was derived by the Department of Health's mathematical modellers, using published empirical data on the efficacy of cleaning and decontamination in removing and inactivating PrPSC and thereby preventing a continuing, self-sustaining epidemic of vCJD, resulting from surgery; it is currently unpublished. Similar approaches have been used to manage the risk of vCJD and BSE in an assortment of settings from blood safety to the permitted constituents of human food and animal feed. A key parameter driving the risk assessment is the prevalence of carriage of the transmissible agent in the UK population. This has been estimated from surveys of appendices, removed surgically, looking for histological changes similar to those seen in cases of vCJD and is around 1 in 2000 for the population whose appendices were removed between 1980 and 1996 [11]. Before it is concluded that lower levels of protein contamination are only required in the UK, it should be remembered that the replication mechanisms first seen in prion proteins have now been identified in other proteins involved in other common neurodegenerative disorders, including amyloid-β in Alzheimer's Disease, α-synuclein in Parkinson's Disease and tau in several different conditions [12]. Further, transmission of amyloid beta has been demonstrated in human growth hormone (HGH) recipients [13,14] including HGH recipients who died of causes other than iatrogenic CJD. If low or absent residual protein on surgical instruments turned out to prevent even a small proportion of cases of Alzheimer's Disease or Parkinson's Disease, given the prevalence of these latter, that would be of enormous public health benefit.

Conflicts of interest statement
None declared.

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References

[1] Perrett D, Nayuni NK. Efficacy of current and novel cleaning technologies (ProReveal) for assessing protein contamination on surgical instruments. In: Decontamination in hospitals and healthcare. Cambridge: Woodhead Publishing; 2014. p. 598—618.

[2] Brown P, Brandel JP, Sato T, Nakamura Y, MacKenzie J, Will RG, et al. Iatrogenic Creutzfeldt—Jakob disease, final assessment. Emerg Infect Dis 2012;18:901—7.

[3] Hillier CEM, Salmon RL. Is there evidence for exogenous risk factors in the aetiology and spread of Creutzfeldt—Jakob disease? Q J Med 2000;93:617—31.

[4] de Pedro-Cuesta J, Mahilho-Fernandez I, Rebano A, Calero M, Cruz M, Siden A, et al. Nosocomial transmission of sporadic Creutzfeldt—Jakob disease: results from risk-based assessment of surgical interventions. J Neurol Neurosurg Psychiatry 2011;82: 204—12.

[5] Bruce ME, Will RG, Ironside JW, McConnell I, Drummond D, Suttie A, et al. Transmissions to mice indicate that 'new variant' CJD is caused by the BSE agent. Nature 1997;389:498—501.

[6] Smith A, Winter S, Lappin D, Sherriff A, McIvor I, Philip P, et al. Reducing the risk of iatrogenic Creutzfeldt—Jakob disease by improving the cleaning of neurosurgical instruments. J Hosp Infect 2018;100:e70—6.

[7] Department of Health. Health Technical Memorandum (HTM) 01-01. Management and decontamination of surgical instruments (medical devices) used in acute care. 2016. London.

[8] Walker JT, Stanton G, Hoffman PN. Latest guidance reflects continuing prion concerns. Health Estate J 2017;October:63—8.

[9] Simmons MD. The protein emperor with no detectable clothes. Med Device Decontam 2018;22:28—32.

[10] Holmes S, McLaughlan E, Winter M. A comparative study of the sensitivity of protein detection test systems for surgical instruments. Zentralsterilisation (Wiesb) 2017;25:296—300.

[11] Gill ON, Spencer Y, Richard-Loendt A, Kelly C, Debaghian R, Boyes L, et al. Prevalent abnormal prion protein in human appendices after bovine spongiform encephalopathy epizootic: large scale survey. BMJ 2013;347:f5675.

[12] Walker LC, Jucker M. Seeds of dementia. Sci Am 2013;308:38—43.

[13] Jaunmuktane Z, Mead S, Ellis M, Wadsworth JD, Nicoll AJ, Kenny J, et al. Evidence for human transmission of amyloid-β pathology and cerebral amyloid angiopathy. Nature 2015;525: 247—50.

[14] Ritchie DL, Adlard P, Peden AH, Lowrie S, Le Grice M, Burns K, et al. Amyloid-β accumulation in the CNS in human growth hormone recipients in the UK. Acta Neuropathol 2017;134:221—40.

R.L. Salmon[1]

Chair Advisory Committee on Dangerous Pathogens, Transmissible Spongiform Encephalopathy Subgroup, C/o Public Health England, 61 Colindale Avenue, London NW9 5EQ, UK

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[1] The views expressed in this Commentary are the authors own.