Calls to tackle protein risk

New techniques in protein detection make it possible to set limits on protein contamination on surgical instruments. In the future, there may be national or local targets on permissible protein residues, but just how much improvement can be reasonably achieved in reducing protein-related infection risk? LOUISE FRAMPTON reports.

Following the publication of research, which estimated that around one in 2,000 people in the UK may carry variant Creutzfeldt-Jakob Disease (vCJD) protein, the Science and Technology Committee recently presented evidence on vCJD and the ongoing risk it poses to the UK.

Ordered by the House of Commons, the meeting took place on 27 November 2013 and heard evidence from a number of experts including Professor Collinge, director of the Medical Research Council (MRC) Prion Unit, UCL Institute of Neurology.

He highlighted the fact that, in addition to the 20,000 or 30,000 people that are predicted to be infected and are carriers in the population at the moment, there are around 6,000 people in the UK who have been notified that they are at increased risk of developing the disease as a result of receiving either blood from a person who went on to develop vCJD or blood products that are implicated, or who have been exposed to contaminated surgical instruments.

Andrew Miller MP, chair of the science and technology committee, said: “More than twenty years on from the BSE crisis, studies have suggested that thousands of people may still carry the infectious agent considered the problematic challenge of detecting and removing residual protein.

Opening the discussion was a presentation on ‘limitations on residual protein contamination on instruments’, by Nigel Tomlinson, who previously advised the Department of Health (DH) on decontamination issues in his role as principal scientific adviser. (He has now retired.)

He explained that residual protein is defined as ‘a mass of protein that remains on an instrument after it has been washed and disinfected, usually in a mechanised way, within a sterile service department’. This potentially poses a risk of protein based infection (such as vCJD), and can affect the acceptability of the instrument for surgical use.

While working for the DH, Nigel Tomlinson received complaints about the functionality of some instruments: “There is a relationship between instrument design and levels of contamination, and the effectiveness of the washing process,” he pointed out.

He acknowledged that the decontamination community would like to see a lower level of bio-molecular protein contamination of instruments at the end of the process and, in an effort to tackle the problem, the DH has adopted a risk-based strategy involving a number of key steps including the investigation of detection and quantification methods, the optimisation of washing and disinfection, and the development of new decontamination techniques.

The first step has included the funding of research into improving protein detection and quantification. There have been a number of pilot studies established to investigate various approaches, with the aim of suppressing vCJD-related risks, within the hospital decontamination setting. The emphasis has been on examining these approaches in practice, rather than simply using a scientific team.

‘Important questions remain to be asked about the potential risk posed by this terrible condition and what the Government should be doing to reduce the spread of infection.’
Sensitive protein detection test

Dr Nanda Nayuni, William Harvey Research Institute, Bart’s & The London school of Medicine and Dentistry, Queen Mary University of London, pointed out that visual inspection and swabbing methods for protein detection are inadequate. He provided an insight into a sensitive protein detection test (ProReveal), which combines a compact fluorescence imaging system and OPA/NAC (o-phthalaldehyde/N-acetyl cysteine) reagent spray.

The process, which takes around five minutes, produces an image of contaminating proteins on an instrument, measures the amount of residual proteins, then indicates a ‘pass’ or ‘fail’ of the decontamination process with an on-screen green tick or red cross. To date, results show that the technology can detect less than 50ng of residual protein on a reprocessed surgical instrument, making this a very sensitive detection method.

The system can be used to optimise decontamination processes and chemistries, within SSDs, as well as by manufacturers in the design of instruments. Most recently, it was announced that detergent manufacturer and supplier, Serchem, is using the test to accurately diagnose the efficacy and optimise the chemistry of its detergents for protein removal.

The test’s ability to detect nanogram levels of protein on surgical instruments is being used by the company’s R&D department in Telford, to test the efficacy of its alkaline, neutral and enzymatic cleaning ranges to remove proteins from specifically calibrated protein soil test standards. Since ProReveal provides quantitative data on residual protein, using the results of these experiments, Serchem’s formulation scientists can assess how effective current detergent ranges are. Using the detection test will also allow them to determine how manipulating components of the detergent’s formulation directly impacts how much protein can be removed, thus making designing an optimum formula for maximum protein removal a quicker and more accurate task.

Paul Arnold, sales director at Serchem, commented: "We supply detergents to over 240 sterile service and endoscopy decontamination sites in the UK alone so we are all too aware of how challenging the need for protein detection technologies with very high levels of sensitivity: ‘We need to be getting down to attomole levels to make a big impact on the risk of vCJD transmission.’ It is also important to be able to ascertain how much protein is present on an instrument – not simply to determine ‘pass’ or ‘fail’, he asserted, adding that there also needs to be an establishment of ‘a convention on calibration’.

As part of this work, there needs to be agreement and standardisation on ‘units’ – are we talking about protein mass per unit area or per instrument? In addition, are we interested in the whole instrument or just the active surfaces – such as blades, which are in contact with the patient? There also needs to be discussion on whether a protein contamination limit could be established nationally or locally. He pointed out that the DH is more likely to take direction from organisations such as the IDSs on such matters and it is unlikely that decisions will be imposed by
the Government, as they have been in the past.

**Prevalence and risk**

Prevalence studies on vCJD have been performed on pathological specimens for around nine years and have shown that the infectious agent remains in the human population.

“The new protein tests are potentially ‘game changing’, because they are sensitive enough to allow you to refine your techniques and remove protein down to a level where you can make some difference to the risk of CJD being transmitted to patients,” Nigel Tomlinson commented.

“The prevalence figure of ‘one in 2,000 people’ with the vCJD protein is not a definitive estimate,” Nigel Tomlinson commented, pointing out that there are a number of risk estimates in circulation. There has been one new clinical case in the UK, in the last two years, and three suspected – but unconfirmed – new cases overseas. The total number of cases in the UK, to date, is 177. Figures for sporadic CJD appear to be showing a slow increase (there are over 80 recorded deaths per year) and this is believed to be highly transmissible, Nigel Tomlinson pointed out.

Better protein detection, combined with improved washing can make a big difference to the risk of transmission, he commented; however, there is currently no data on typical levels of contamination on a wide range of instrument types and the question remains of just how much improvement can reasonably be achieved.

“A lot of improvement does not require great cost – just additional work and care,” he asserted. He went on to explain that contamination levels are dependent on instrument design, but improvements in protein removal can be achieved through the optimisation of washer disinfector settings, choice of detergent, alkalinity (which is known to be helpful in destroying CJD infectivity), as well as enzyme activity.

Although the latter is known to be helpful, there are some parts of the CJD molecule which are resistant to enzyme action. In addition, particular care should be taken in protein detection and washer disinfection when reprocessing instruments used on high risk tissues (e.g. brain surgery and posterior eye surgery).

**The future: setting limits**

In the future, protein limits will be set, either nationally or locally. Nigel Tomlinson concluded: “Most people I have spoken to say they want a hard target...It is, in my opinion, feasible to use the new protein detection methods to proceed towards lower contamination levels. I would challenge you as to why this is not a desirable aim, as there appears to be no cost implications – it is simply a matter of some thoroughness in the way we do our work and requires collaboration with national or local scientists to ensure the optimisation of the washer disinfector and its chemistry.”

In terms of a possible ‘traffic light’ approach to risk, he suggested that 200 micrograms per instrument could be defined as ‘red’; 50-200 micrograms would be ‘amber’ and below 50 micrograms would be ‘green’.

“Most departments could achieve this quite quickly,” he commented. However, he added that research at GOSH and St Bart’s suggests that it would not be difficult to achieve even lower levels – a ‘green’ limit of 5 micrograms per instrument may be defined in the future, therefore.

“At this point, the threshold is crossed where there is virtually no risk of vCJD transmission for surgery, involving low and medium risk tissues, as the risk is being dealt with by the decontamination unit. In this case, you will be doing society a very big favour in dealing with a disease that we understand very poorly. This is a readily achievable objective,” Nigel Tomlinson continued. “I cannot tell you if this will become policy, but professional and learned bodies can influence the derivation of targets and I would ask you to think hard about doing this.”

The IDSc conference and exhibition took place at the Hilton, Blackpool, 2-4 December 2013.

**References**

