

Variant Creutzfeldt-Jakob Disease (vCJD) and Gastrointestinal Endoscopy

A. T. R. Axon, U. Beilenhoff, M. G. Bramble, S. Ghosh, A. Kruse, G. E. McDonnell, C. Neumann, J.-F. Rey, K. Spencer

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Variant Creutzfeldt-Jakob disease (vCJD) is a transmissible form of spongiform encephalopathy believed to be contracted from the consumption of bovine spongiform encephalopathy (BSE) infected beef products. To date over 100 individuals have developed this incurable disease. There have been no documented cases of iatrogenic infection, but there is a theoretical risk that surgical procedures could transmit the disease. This review describes the background of the disease and assesses the possible risks of transmission through endoscopic procedures. The risk of transmission by endoscopy is small and probably negligible if suitable procedures are followed. The greatest potential danger arises from healthy individuals who are incubating the disease. Pathological prions (PrP^{sc}) may be found in lymphatic

tissue of these individuals (particularly tonsils), but smaller amounts have been identified in the appendix and Peyer's patches. These prions are resistant to all forms of conventional sterilization. There is a theoretical risk that biopsy forceps and the operating channel of endoscopes could become contaminated. This review gives recommendations as to how these small risks can be minimized. They include the employment of single-use forceps for biopsies taken from the terminal ileum, greater attention to the maintenance of endoscopic equipment and accessories, more rigorous manual cleaning of endoscopic equipment and the use of well designed, disposable cleaning brushes for the operating channel of the endoscope.

Introduction

vCJD is a fatal disease of humans, which is believed to have originated from the consumption of food derived from beef products containing the BSE agent. The infectious particle is a malformed prion protein that is capable of stimulating a catalytic reaction whereby native prions develop the abnormal folded structure, leading to the typical spongiform pathology in the brain. The abnormal prion is resistant to all conventional forms of sterilization and is not denatured by cooking or hydrolyzed by digestive enzymes. To date over 100 individuals are known to have contracted the disease, but in view of the long incubation period of the condition it is unclear how many people in the population are incubating this disease. Although the condition is mainly confined to the United Kingdom, a few cases have been reported in the Republic of Ireland and in France. The incidence of the disease is continuing to rise.

A number of prion diseases other than vCJD affect human beings and lead to similar pathological changes in the brain. It is known that these can be transmitted by neurosurgical instruments. To date no case of vCJD has arisen iatrogenically, however the theoretical possibility that this may occur does exist. Public health authorities and those societies and institutions responsible for providing guidelines for good practice should be alive to this possibility and offer advice concerning the risk to health and how the risks may be minimized.

The European Society of Gastrointestinal Endoscopy represents the digestive endoscopy societies of 40 countries. Digestive endoscopy is a procedure where flexible optical instruments are passed through the mouth or the anus into the gastrointestinal tract. They are primarily used to inspect its lining, but an essential part of most examinations is the removal of tiny pieces of tissue for pathological examination under the microscope. In addition many operations are performed through these instruments using equipment passed through the operating channel. The development of endoscopy has provided enormous benefits to patients by early and accurate diagnosis of disease, and serious conditions can be treated much more simply, safely, cheaply, and effectively using endoscopic methods than by the open sur-

gical methods that were used previously. Endoscopy is an essential medical procedure for most individuals suffering from or having significant symptoms attributable to the gastrointestinal tract.

Flexible endoscopes are inherently difficult to sterilize because they are damaged by high temperatures and strong chemicals. In the past certain infectious diseases (including hepatitis B) have occasionally been transmitted by endoscopy. This has led to stringent recommendations concerning the reprocessing of equipment between each use. When these procedures are followed the risk of infection from viruses, bacteria, fungi, and parasites is virtually negligible; however, no form of sterilization in current use (even for autoclavable instruments) is capable of completely destroying the prions that are responsible for vCJD. In the United Kingdom the Department of Health has indicated that because of the theoretical risk of transmission by surgery, tonsillectomy, if indicated, has now to be performed using disposable, surgical equipment.

Concerns have been raised in the press by health providers and by endoscopists as to whether there is a risk of prion transmission by endoscopy. The ESGE therefore convened a Working Party with a remit to consider the potential risk of transmission of prion disease through endoscopy and to make recommendations as to how this potential risk might be reduced. It must be emphasized that there is no evidence to suggest that any case of prion disease has ever been transmitted in this way, however, vCJD is a new disease and one, which is likely to become more prevalent in the future.

Methodology

The problem of vCJD was considered at a meeting of the Guidelines Committee of ESGE on Friday 9 February 2001. A Working Party was convened and met on Wednesday 11 April 2001. A draft document was produced and circulated to all members of the Working Party who were asked to contact any other individual they thought should provide further input. A second document was discussed at the meeting of the Guidelines Committee of the ESGE on Friday 6 July 2001. A final document was prepared and approved by all members of the Working Party and Guidelines Committee for publication on behalf of the ESGE. It must be emphasized that this report is based on current knowledge, which may change.

Prions and Human Transmissible Spongiform Encephalopathy (TSE)

Background

What are the TSEs?

The term prion is used to indicate infectious proteins [1]. Prusiner first coined the term and formulated the hypothesis that the TSEs are caused by small proteinaceous infectious particles. TSEs are a group of fatal neurodegenerative

diseases affecting animals and human beings. The human TSEs [2] are shown in Table 1. The most common human TSE is Creutzfeldt-Jakob Disease (CJD) with an incidence of 0.5–1.5 new cases per million per year [3]. However, it is the relatively newly diagnosed *Variant* CJD (vCJD) that has attracted media attention.

Table 1 Human Transmissible Spongiform Encephalopathies

Creutzfeldt-Jakob Disease (CJD)
Sporadic (85 %)
Familial (10 %)
Iatrogenic (5 %)
Variant CJD (vCJD)
Kuru
Gerstmann-Strausler Syndrome (GSS)
Fatal Familial Insomnia (FFI)

Bovine spongiform encephalopathy (BSE) was first described in 1986 and made a notifiable disease in 1988; the likely source of BSE was meat-and-bone meal produced by rendering discarded animal fat, bones offal, whole carcasses, and other material from bovine, ovine, porcine, poultry and other sources [4]. vCJD was first reported in 1996 [5], and serious consternation resulted from evidence linking it to the exposure of humans to the BSE agent. Dietary exposure the most likely source of infection, was a result of BSE affected bovine CNS tissue entering the human foodchain.

What is a Prion?

Prions consist solely of proteins and the unusual “infectious” agents are a rogue form of a widely distributed normal prion protein. The human prion protein is coded by a single gene (*PrP*) located on the short arm of chromosome 20 [6]. The product of the mRNA is a 253 amino acids long copper binding glycoprotein, and consists of 5 amino-terminal octapeptide repeats, 2 glycosylated sites and 1 disulphide bridge. Two signal sequences in the amino- and carboxy-terminal ends are removed during processing and the prion protein is attached to the outer surface of the cell membrane by a glycosyl-phosphatidyl-inositol (GPI) anchor [7]. The *PrP* gene is constitutively expressed in the brain and other tissues of healthy animals and normal humans. This normal host encoded prion protein is called cellular prion protein (PrP^c). The infectious pathological malformed isoform is called scrapie-associated prion protein (PrP^{sc}). PrP^c and PrP^{sc} have identical amino acid sequences and similar pattern of glycosylation but differ in their secondary structure [1]. PrP^c is soluble, protease-sensitive and is completely degraded by limited protease digestion. PrP^{sc} is the protease-resistant form found in the disease setting, such as vCJD and is stubbornly insoluble. The resistance of PrP^{sc} to proteolysis by the gastrointestinal tract might be an important factor in transmission by allowing intact prion protein to come into contact with ileal mucosa. The post-transla-

tional conversion of PrP^c to PrP^{sc} represents the central event in all TSE pathogeneses, including vCJD. No covalent differences have been found between PrP^c and PrP^{sc} to account for these post-translational modification [8]. Biophysical studies have demonstrated a striking conformational difference between PrP^c and PrP^{sc} – the α -helical content of PrP^c is 40%, with little or no β -sheet, whereas PrP^{sc} contains 50% β -sheet and only 20% α -helix [9].

Experiments with transgenic mice show that mice lacking the *PrP* gene are not able to propagate infectivity and develop the disease [10]. Prion replication occurs when ingested PrP^{sc} interacts specifically with host PrP^c, catalysing its structural conversion to the pathogenic form of the protein PrP^{sc}[11]. This catalytic reaction has also been shown *in vitro* by *de novo* generation of PrP^{sc}-like molecules after mixing purified PrP^c with PrP^{sc}[12]. The exact mechanism underlying the conversion is uncertain. Both a template assisted conversion model [11] and a nucleation-polymerisation model [13] have been proposed as conformational transmission of protein misfolding.

How Many People will be Affected?

There is considerable speculation and uncertainty about the size of the epidemic and the likely number of vCJD cases. It has been suggested that the current mortality data are consistent with between 63 and 136000 cases among the population known to have a susceptible genotype [14]. Around 40% of the population have 2 copies of the methionine codon at codon 129 of the *PrP* gene and are considered susceptible. Other genotypes however may merely have longer incubation periods. The National CJD Surveillance Unit [15] has prospectively identified 102 patients with vCJD up to June 2001 in Great Britain, the vCJD incidence was higher in the North of Great Britain than in the South. Though vCJD is considered a disease of the young, elderly people may also be affected [16]. The BSE agent has contaminated humans not only in UK but also in the Republic of Ireland and in France. Therefore potential risk of transmission exists worldwide, regardless of National BSE incidence.

How Does the Prion Enter Through the Intestine?

This has recently been reviewed [17]. Early presence of infectivity [18] and PrP^{sc}[19] in the aggregated intestinal lymphoid follicles (Peyer's patches) after oral exposure to the TSE infectious material suggests that these are the most probable sites for the intestinal uptake of prions. The 37-kDa Laminin Receptor Precursor (LRP) has been identified as a putative receptor for prion proteins [20], and brush border expression of the mature 67-kDa Laminin Receptor (LR) has been found in approximately 40% of human small intestinal mucosae [21]. The anatomical and cellular distribution of PrP gene and PrP^c protein in human enteric ganglia and neuronal elements of the small intestinal mucosa in patients with no clinically manifest neuropathology has been recently described [22]. Using PrP-

specific monoclonal antibodies, strong reactivity could be detected in frozen sections of small intestinal tissues, thus demonstrating expression of PrP^c in different elements of the enteric nervous system (ENS). Confocal microscopy confirmed the presence of PrP^c in nerve fibres and in enteric glial cells. *In situ* hybridisation demonstrated PrP mRNA both in nerve cell bodies and in glial cells within the ENS ganglia. Intimate association of PrP^c-positive nerve endings with epithelial cells indicates that only a thin epithelial layer stands between ingested TSE-agent and host PrP^c in the ENS. The presence of the 37-/67-kDa LR in the brush border of intestinal epithelium may represent a risk factor for oral TSE susceptibility enabling transfer of the "infectious" agent across the human intestinal epithelium to the adjacent PrP^c-positive nerve endings. Direct evidence for this hypothesis is however lacking.

Which Human Tissues Harbour Prions?

The protease resistant form of PrP (i.e. PrP^{sc}) can be detected in the brain and spinal cord of vCJD victims, as expected, but positive staining can also be detected in follicular dendritic cells within germinal centres of the tonsil in a widespread distribution. A more restricted pattern of positivity could be detected in the appendix, spleen and lymph nodes from the cervical, mediastinal, para-aortic, and mesenteric regions [23]. Positive staining was also identified in cells that corresponded to follicular dendritic cells in Peyer's patches in the ileum, although marked autolysis prevented a detailed analysis and immunophenotyping. The oesophagus, stomach, liver, gallbladder, pancreas, kidneys, and pelvic organs were negative for immunostaining in vCJD. In one patient, PrP^{sc} was detected in an appendix removed in 1995, 8 months before onset of symptoms [24]. A recent report using high sensitivity immunoblotting in four patients with neuropathologically confirmed vCJD detected the presence of PrP^{sc} in tonsil, spleen, and lymph nodes. The concentrations of PrP^{sc} in these tissues were 0.1% – 15% of those found in brain. Tonsil consistently had the highest concentrations. Other peripheral tissues studied were negative for PrP^{sc} with the exception of low concentrations in rectum, adrenal gland and thymus from a single patient with vCJD. vCJD appendix and blood (buffy coat fraction) were negative for PrP^{sc} at the level of assay sensitivity (up to 5nL 10% vCJD brain homogenate). Stomach, small intestine, and colon other than rectum were not examined [25].

A "look back" study using a sensitive immunohistochemical technique failed to detect pathological PrP after proteinase K digestion in a retrospective series of over 3000 appendix specimens and 95 tonsil specimens [26] but prospective studies using Western blotting are still underway.

In all sporadic cases of CJD, lymphoid tissues and other organs gave a negative reaction to PrP. Therefore only cases of vCJD have PrP resistant to protease digestion, equivalent to PrP^{sc}, detectable outside the central nervous system in lymphoid tissues.

What is the Infectivity of Human vCJD Affected Tissue?

There are currently scant data available to address this issue adequately. Lymphoid tissue in experimental models of prion disease are on average 1–2 logs less infective than the brain and spinal cord [27]. Information on the infectivity of intestinal tissue from vCJD patients is currently not available. Recent data on detection of vCJD infectivity in extraneural tissue from two affected patients suggest that spleen and tonsil samples transmitted to only a proportion of challenged mice inoculated intracerebrally. Incubation periods were relatively long indicating lower infectivity levels than vCJD affected brain tissue which transmitted to all challenged mice. vCJD affected brain contained between a hundred to thousand times more infectivity than spleen. Buffy coat and plasma from these two vCJD patients failed to transmit disease to the challenged mice. Direct intracerebral inoculation should not however be equated with transmission via intact or damaged gut tissue [28]. Whole blood from one of 11 seemingly healthy sheep incubating BSE (infected by the oral route with brain from a diseased cow) was able to cause the disease when transfused into another sheep [29]. The UK National Blood Transfusion Service has already implemented leucodepletion of donated blood and imports all plasma derivatives from BSE free countries. No further measures are possible within the realms of feasibility.

Primate transmission experiments using brain homogenates from a French patient and 2 British patients with vCJD suggests that the BSE agent rapidly adapts to primates accompanied by enhanced virulence [30]. That the pathogenic properties of the BSE agent for primates are enhanced by primary passage through humans is a disturbing fact of direct relevance to iatrogenic transmission of the agent.

Could Endoscopy Transmit CJD?

Gastrointestinal endoscopy may be a necessary procedure for some patients with either sporadic (sCJD) or “new variant” (vCJD) where no feasible alternative exists. Procedures involving disruption of tissue pose the greatest threat to endoscope contamination, in particular biopsy or disruption of lymphoid tissue. Patients who are incubating vCJD but in the pre-clinical phase of their illness are the most likely source of person to person transmission.

Sporadic CJD

In sporadic CJD, abnormal prion protein is largely confined to the central nervous system and spinal cord although the posterior eye is also a potential source of iatrogenic transmission. The first reported case of iatrogenic transmission of CJD involved a corneal transplant. Gastrointestinal endoscopy does not result in contact between the endoscope or accessories (such as biopsy forceps) with infected tissues, which have the potential to transmit the disease. It follows that gastrointestinal endoscopy is unlikely

to be a vector for the transmission of prions from one individual to another and endoscopes used on patients with sCJD can be returned to use following normal thorough cleaning and disinfection [31].

Variant CJD

The situation in vCJD is different. Animal models show that the lymphoreticular system throughout the body contains the mutated prion protein (PrP^{sc}) for most of the incubation period [19]. There are moderately high levels of PrP^{sc} in the tonsils and other lymphoid tissue such as Peyer’s patches or germinal centres in the wall of the appendix [24,32]. In animals PrP^{sc} has been reported in the intestinal epithelium [33,34] and enteric nervous system cells [17] where it accumulates prior to being detectable in the central nervous system [34]. Only the epithelium stands between the endoscope and potentially infectious tissue of the gut lymphoid system [17]. It is therefore theoretically possible to transmit prions from one individual to another if an endoscope is contaminated with lymphoid tissue and is then inadequately decontaminated. The theoretical risk is different for upper and lower gastrointestinal endoscopy and relates to potential contact with lymphoid tissue (although villus epithelium itself could represent a risk factor [19,33]). It is the act of taking a biopsy, which poses the greatest threat for endoscope contamination and possible iatrogenic spread.

Upper Gastrointestinal Endoscopy

Already Diagnosed Cases

The tonsils could in theory contaminate the outer sheath of the endoscope if traumatized. Biopsy of stomach and duodenum are also theoretical risks to the biopsy forceps and operating channel. In known or strongly suspected vCJD all possible ways of avoiding gastroscopy should be explored. The commonest reason for requesting a gastroscopy will be to place a percutaneous endoscopic gastrostomy feeding tube when naso-gastric feeding has failed. Provided that no alternative exists (such as ultrasound guided placement) gastroenterologists should seek an instrument that has already been used on such a patient previously. If no such instrument exists then the person performing the endoscopy should inform the national society representing endoscopy, so that this instrument can be used in other patients with CJD in similar situations. An alternative is to use a gastroscope, which is approaching the end of its useful life. Such an instrument can then either be destroyed or quarantined until required for another patient with vCJD. Countries with a high incidence of vCJD may need to keep several gastroscopes for this purpose.

Patients Incubating vCJD

Undiagnosed patients incubating vCJD may pose the greatest threat of person to person transmission because their condition will not be known at the time of endoscopy. We

believe that the risk of transmission will be small but may not be zero. To date none of the 3000 appendices or tonsils removed from the normal population have been positive for PrP^{sc}[26]. The risk of endoscopy on an infective patient therefore is unlikely to be greater than 1 in 3000 and may be much less. A very small risk however could be decreased by good endoscopy technique avoiding traumatic intubation which may damage the mucosa overlying the tonsils and allow lymphatic tissue to come into contact with the external surface of the endoscope. Biopsies taken from intestinal mucosa may contain lymphoid tissue. Damaged or inferior biopsy forceps, which tear rather than cut the tissue being sampled, might increase the small risk of contaminating the operating channel of the endoscope. If contaminated biopsy forceps were used again following inadequate decontamination they could pose a theoretical chance of transmission. Tissue protruding outside of the biopsy cusp might contaminate the operating channel or valve of the gastroscope, which itself might then become a vector for disease transmission if inadequately decontaminated. In this context the taking of multiple samples on one insertion of the biopsy forceps may overload the cusp and lead to channel contamination.

It follows that non-traumatic intubation under direct vision, the use of properly maintained equipment and avoidance of unnecessary biopsy will reduce the risk. Thorough cleaning of all equipment will diminish the risk further but reliance on disinfectants would be misplaced. The best protection against the transmission of PrP^{sc} by endoscopic equipment is probably repeated manual cleaning of the biopsy channel using a purpose designed brush in good condition and appropriately sized for the specific channel followed by reprocessing machine decontamination.

Lower Gastrointestinal Endoscopy

As with gastroscopy the principle for all examinations should be to minimise potential contamination of the endoscope by "best practice". Biopsy forceps should be functioning optimally. Thorough cleaning of the colonoscope is the cornerstone of any policy designed to reduce the potential transmission of vCJD via endoscopy. Worn out and inappropriate sized cleaning brushes must not be employed prior to reprocessing. Valves could also become contaminated and should be properly cleaned and reprocessed. It would be helpful if disposable caps for the operating channel could be provided at acceptable cost.

Biopsied Peyer's patches in the ileum pose the greatest theoretical risk in colonoscopy. Remembering that the greatest potential risk arises in undiagnosed patients it follows that ileal biopsy should be avoided unless clinically indicated. If biopsies are taken from the ileum, disposable forceps should be used.

ERCP

ERCP is unlikely to represent any greater risk of prion transmission than upper GI endoscopy. Standard recommended procedures for cleaning and reprocessing must always be performed.

The Risk of Transmission of vCJD By Aspiration of Blood

As indicated earlier in this review the levels of infectivity present in the blood in vCJD are unknown, but are likely to be less than in brain or lymphoid tissues. The quantity of blood left within an endoscope after proper cleaning and rinsing is negligible compared with that given in a blood transfusion. It therefore seems unlikely that transmission of vCJD by aspiration of blood into the endoscope is a major risk.

Resistance of PrP^{sc} to Conventional Disinfection and Sterilization Techniques

Prions demonstrate significant resistance to routine physical and chemical disinfection or sterilization methods. They are biochemically unique in their intrinsic resistance to methods used to inactivate proteins, including proteases, detergents, and heat [35]. It is important to note that the reports in the literature of prion resistance and prionocidal efficacy vary considerably, which is due to differences in methodology, prion strains used, processes or formulations tested, etc. Based on a review of the current literature, a summary of techniques shown to be effective or ineffective is given below [35–39] (Table 2):

Table 2 Effectiveness of disinfection techniques for PrP^{sc}

Effective Techniques	Ineffective Techniques
Incineration	UV, ionizing and microwave radiation
Prolonged steam sterilization ≥ 121 °C for ≥ 30 minutes (gravity displacement) 134 °C for ≥ 18 minutes (prevacuum)	Acids, including HCl
Sodium hydroxide (1–2M at > 1 hour)	Glutaraldehyde, OPA, Formaldehyde
Sodium hypochlorite (2 % available Cl, 1 hour)	Ethylene oxide, Alcohols
Some phenol formulations	Hydrogen peroxide, chlorine dioxide
Formic acid (96 %, for histological samples)	Dry heat
Peracetic acid (under some conditions)	Boiling, desiccation, freezing
Guanidinium hydrochloride or isocyanate	Most phenolics, quaternary ammonium compounds and iodophors Enzymes (including proteases)

Because prions do not have associated nucleic acids, any techniques that target nucleic acids (DNA or RNA) are ineffective and include UV and other radiation methods. Any biocides that demonstrate protein cross-linking as a mode of action (aldehydes, ethylene oxide, alcohols) are not effective and may increase the risk to patient by further fixing prion contaminated material onto a given device [40]. Prions are generally more susceptible to alkali than acid, with 1M sodium hydroxide reported as effective at 1 hour [41]; however, other investigators have reported detection of residual prions following treatment at 1M or 2M NaOH [42,43]. Similar conclusions may be drawn from a review of reports on the effectiveness of gravity drain or pre-vacuum autoclave cycles [38]. Some oxidizing agents have also been shown to be effective, including sodium hypochlorite (bleach) [44] and peracetic acid in formulation [36]. It is important to note that no one method has been shown to be 100% effective against prions and that the most prudent suggestions for medical device reprocessing are a combination of methods, including adequate cleaning, chemical disinfection, and chemical or physical sterilization [38,39]. These methods generally include a thorough manual cleaning, followed by soaking in high concentrations of sodium hydroxide or sodium hypochlorite and then autoclaving for extended periods [37,45–47].

Practical Measures for Preventing the Spread of vCJD by Flexible GI Endoscopy

No conventional sterilization methods can successfully destroy PrP^{sc}, the infecting agent in vCJD. However, the likelihood of endoscopic equipment becoming contaminated with infective tissue is small and the application of rigorous cleaning techniques will reduce the risk even further. The amount of prion protein required to infect a patient through the intestinal route is unknown. Even the small quantities that could theoretically contaminate the biopsy jaws may not reach the patient when taking a biopsy because the tissue in contact with the cusp of the forceps is removed at the time of biopsy and is not left within the intestine. Needles are potentially more of a concern even though they are inserted through the endoscope within a teflon cover. Previous recommendations from this Society state that all needles used in endoscopy should be disposable.

It should be emphasized that aldehydes, such as glutaraldehyde, fix protein. They should never be used for disinfection until the equipment has been thoroughly cleaned and washed with detergent and rinsed with water. If the cleaning process is performed assiduously the risk of prion contamination of endoscope channels will be minimized.

A detailed addendum prepared by ESGENA is attached to this review and outlines special nursing precautions that should be taken.

It is important for endoscopists to recognise the potential for transmission through poor practice. It is very much a

team effort by all those involved in the endoscopy unit to minimize contamination and maximize cleaning. Best practice defined in these terms will reduce a very small, potential risk to one which can currently not be measured. There have been no reported cases of vCJD transmitted by endoscopy in the UK, but it would be wrong to become complacent. There is no substitute for vigilance in maintaining or improving standards which will protect patients against the iatrogenic transmission of this devastating disease.

Future Trends in the Design of Endoscopic Equipment

Endoscopes

Endoscopes used in gastrointestinal endoscopy have been developed to meet the established hygienic requirements of health care providers, users and patients. Existing reprocessing methods, manually or by automatic machines, have been microbiologically validated.

Until very recently, it had been considered unnecessary to take into account the potential involvement of prions during flexible endoscopy procedures.

Modern flexible fiberoptic and video endoscopes, are by their nature, complex and somewhat delicate instruments. As such, the aggressive chemicals needed to deactivate prions normally imply severe damage for these instruments.

The nature of prions, and the impossibility of their deactivation by “traditional means” – cold fluid disinfection and sterilisation, thermo-chemical reprocessing, even autoclaving, implies a greater need to be able to remove all debris from endoscope surfaces, internal and external; in short, manufacturers must carefully consider the subject of cleanability, prior to any disinfection/sterilisation processes.

This represents one of the new challenges facing manufacturers: the need to validate cleaning processes independently, and not just validate a complete reprocessing procedure.

Consideration must therefore be given to future design aspects of endoscopes, which may support and/or enhance cleanability. For example, it would be desirable if channels that are actively exposed to debris from the intestinal lumen could be made accessible for mechanical brushing. Research should also focus on materials which minimize the accumulation of debris from the intestinal lumen. It must be acknowledged that significant design changes cannot be incorporated into sophisticated medical equipment within a short time and this implies a need to consider such potential modifications in “next-generation” developments.

For the present, apart from validating the efficacy of cleaning methods for the types of endoscopes currently in use, more conscientious and effective brushing of biopsy channels, with immediate disposal of worn out, damaged or in-

effective cleaning brushes is indicated; in fact, cleaning brushes should be regularly discarded, probably on a daily basis – single-use cleaning brushes can be considered as the optimum choice. Actions by manufacturers to enhance the cleaning action/s of the brushes are certainly to be encouraged.

Whether the proposed cleaning validations/improvements will demonstrate consistently complete removal of protein from all endoscopes is currently a matter for conjecture. There may however be the possibility of assuring a certain limited level of compatibility for flexible endoscopes with some recommended chemicals known to successfully deactivate prions; whilst this may *de facto* increase repair and maintenance costs, it would certainly be more economic than having to dispose of these expensive instruments. (The individual endoscope manufacturers should be contacted for further technical information.)

Regular channel exchange (aimed at minimising the difficulty of cleaning damaged or worn channel surfaces) can be provided by all endoscope manufacturers, either during normal overhauls, or at regular intervals – probably at least once every year is to be recommended. (The individual endoscope manufacturers should be contacted for further information.)

Modifications to biopsy procedures, as indicated elsewhere, may be helpful; improvements in biopsy devices aimed at minimising or eradicating potential contamination of the channels may also be indicated.

Endotherapy Devices and Accessories

Certain other accessories may need careful review and might ultimately need to be considered and be made available as single-use items.

In general terms, there does not seem to be any current indication to recommend widespread implementation of single-use endotherapy devices. Nevertheless technical improvements are required so the biopsy forceps cut rather than tear mucosa so as to ensure that all specimens are kept within the jaws of the forceps. It may be possible to produce multiple suction biopsy forceps where specimens are brought out into an accessories own channel rather than directly into the operating channel of the endoscope.

While there are many differing views and calculations concerning the economics of single-use versus reusable items, it can safely be said that increased security and convenience always has a price and it would be regrettable if any reaction in terms of movement to single-use products, not adequately supported by scientific evidence and increased funding, were to result in reduction of endoscopy services available to patients in need of such diagnostic and therapeutic procedures.

The Members of the ESGE Guidelines Committee are as Follows:

Professor A. T. R. Axon
 Mrs. U. Beilenhoff
 Mr. H. Biering
 Mrs. D. Duforest-Rey
 Professor M. Jung
 Mr. P. Jurkowski
 Mrs. I. Kircher-Felgentreff
 Mr. P. Klasen
 Dr. A. Kruse
 Mr. J. Mills
 Mrs. C. Neumann
 Mr. A. Papoz
 Dr. M. Pietsch
 Professor T. Ponchon
 Mrs. S. Popovic
 Dr. J.-F. Rey
 Mr. K. Roth
 Mrs. A. Schuster
 Mr. B. Slowey
 Mr. K. B. Spencer
 Mr. M. Stief
 Mr. D. Wilson

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Addendum – The European Society of Gastroenterology and Endoscopy Nurses and Associates (ESGENA)

Recommendation for the Reduction of the Risk of Transmission of Prions in Endoscopy

This document is supplemental to the previously published ESGE/ESGENA Reprocessing Guidelines

Introduction

As there are no known effective means of disinfection or sterilisation following exposure to prions the emphasis in preventing transmission of prions in endoscopy must be on the removal of organic matter from equipment and the prevention of cross contamination of the environment.

I. Staff Safety

- Endoscopes and accessories are a potential source of infection. Therefore validated and standardised reprocessing according to manufacturers' recommendations is essential. This requires special training and knowledge. Staff should be trained in
 - care and maintenance of equipment
 - handling of equipment during procedures
 - reprocessing of equipment, including cleaning, disinfection and sterilisation
 - infection control, including potential health risks.
- Reprocessing of endoscopic equipment should only be undertaken by trained and competent staff.
- Reprocessing of endoscopic equipment should be undertaken in a separate, dedicated reprocessing room to minimise the risk for other personnel and the general public.
- During reprocessing of equipment staff should wear protective clothing (gloves, long sleeve moisture resistant gowns, masks/visors) to protect themselves from splashes, aerosols and vapour.

- A small pipette, pair of tweezers or single-use toothpick should be used to remove biopsy specimens from the biopsy forceps cup (*Using a needle increases risk of needle stick injury*) or specimens may be removed by agitating the forceps cup in NaCl 0.9%;
 - do not use needles to remove specimens
 - do not dip the biopsy forceps cup directly into formaldehyde solution. (Aldehydes denature and fix organic material. This may impair the subsequent cleaning of forceps.)
- Rinse the biopsy forceps cups in NaCl 0.9% or tap water before taking the next biopsy in order to avoid re-transfer of organic material into the biopsy valve or endoscope channel.

II. Choice of Accessories

- **Biopsy forceps**
- Disposable/single use biopsy forceps should be used for ileum biopsies.
- Disposable biopsy forceps reduce the risk for
 - staff as no reprocessing is required, and for
 - patients as they have not been previously exposed to potentially infective organisms during endoscopic or reprocessing procedures.
- **Endoscopic injection needles** should be disposable in order
 - to minimise the risk to endoscopy personnel (needle stick injuries)

- to avoid problematic reprocessing. (The narrow lumen of injection needles does not allow effective reprocessing.)
- **Cytology brushes** should be disposable as they cannot be cleaned effectively. Tissue residue may remain on the brush, potentially causing
 - transmission to the next patient (exogenous infection) or
 - incorrect cytological diagnosis.
- **The use of disposable invasive accessories** should be encouraged when possible in order to
 - minimise the risk to endoscopy personnel
 - avoid potentially problematic reprocessing.
- **Cleaning brushes** should be disposable because brushes cannot be cleaned effectively. Tissue residue may remain on the brush, and be transmitted onto the next piece of equipment reprocessed, with all adherent consequences.

III. Utilisation of Accessories During Endoscopic Procedures

- Disposable gauze/sponge should be used when accessories (especially biopsy forceps/invasive accessories) are withdrawn from the instrument channel and removed from the endoscope in order
 - to remove secretions
 - to wipe clean external surfaces of the equipment
 - to avoid splashing while removing accessories from the instrument channel in order to minimise contamination of the environment and staff.
- A separate instrument table/trolley to deposit accessories during procedures and for the removal of specimens from accessories should be used in order
 - to avoid contamination of surroundings
 - to ensure adequate space for safe handling.
 Instrument trolleys should be covered with disposable, waterproof sheets which can be discarded after each procedure.

IV. Reprocessing of Equipment

Key points for reprocessing endoscopic equipment are as follows:

- Aldehyde containing cleaning agents must not be used for cleaning as they denature and fix proteins, and this may impair effective cleaning.
- Alkaline detergents or enzymatic type detergent solutions or NON-COAGULATING disinfectants with good cleansing power are recommended for the cleaning of endoscopic accessories.
- Endoscopic equipment should be reprocessed IMMEDIATELY after removal from the patient in order to avoid the drying and fixation of organic material.
- Thorough manual cleaning is a prerequisite for effective decontamination. Therefore manual cleaning must always take place before disinfection or sterilisation.
- Cleaning and rinsing solutions should not be re-used.

Accessories

- Manual cleaning is the most important step in the removal of organic material from accessories. This includes thorough cleaning by
 - dismantling of accessories as far as possible (follow manufacturers recommendations)
 - cleaning of external surfaces by using a soft, disposable cloth/sponge and brushes
 - thorough brushing of the biopsy forceps' cups
 - flushing all available channel lumens.
- Ultrasonic cleaning is essential for the removal of debris from inaccessible spaces of complex accessories such as spiral biopsy forceps:
 - do not overload the tray of the ultrasonic cleaner in order to avoid ultrasound "shadows"/dead space
 - use dedicated ultrasonic solutions (**NOT** aldehyde containing detergents). Ultrasonic cleaning is recommended for 30 minutes, 35–47 kHz, 40–60 °C).
- After thorough rinsing and drying, endoscopic accessories should be sterilised in accordance with manufacturers' instruction (recommendation: steam autoclave, 134 °C, 5 minutes, pre-vacuum).

Endoscopes

- Thorough manual cleaning with detergent remains the most important step of the endoscope reprocessing procedure. This includes
 - cleaning of all external surfaces by using a soft, disposable cloth/sponge, and brushes
 - cleaning of valve ports, channel opening and suction ports with a suitable brush and cotton bud
 - brushing of all accessible channels with a flexible, purposed designed brush. Appropriate sized brushes for each channel have to be used to ensure good contact with the channel walls
 - flushing of all lumen.
- Select appropriate size and type of cleaning brush in accordance with size and type of endoscope channels.
- In order to ensure maximum effectiveness of cleaning brushes
 - single use brushes or
 - change of brushes on a daily basis are recommended.
- All reusable brushes have to be thoroughly cleaned manually, followed by ultrasonic cleaning, and decontaminated (preferably sterilised) after each usage.

V. Automated Reprocessing Systems

- Thorough manual cleaning of equipment, especially small equipment channels, is a prerequisite for effective disinfection – independent of whether a manual or automatic reprocessing cycle is performed.
- The use of automated reprocessing after manual cleaning is recommended in order

- to provide a standardised and validated reprocessing cycle in a closed environment
 - to minimise staff contact with chemicals and contaminated equipment
 - to minimise the contamination of the environment.
- Machines may pose an additional infection risk. Therefore they must
- be cleaned and maintained according to manufacturer's recommendation on a daily base
 - have regular engineering maintenance
 - undergo regular microbiological surveillance.

- Machines must be capable of self-disinfection and should use bacteria free/sterile rinsing water.
- Machines should not re-use the cleaning and rinsing water.

The previously published ESGE-ESGENA Guidelines on Cleaning and Disinfection in GI Endoscopy have to be adhered to (Endoscopy 2000; 32: 77–83).

Corresponding Author

A. T. Axon
Div. of Gastroenterology
The General Infirmary
Great George Street
LS1 3EX Leeds
United Kingdom

Fax: +44-113-392-2125
E-mail: anthony.axon@leedsth.nhs.uk