What is already known on this topic

A recent prevalence study of accumulation of prion protein (as a marker for vCJD infection) in appendix and tonsil specimens in the UK found 3/12 674 positive cases, which is more than expected from the current number of clinical cases of vCJD

What this study adds

Analysis of DNA from two of the three positive samples found them to be valine homozygotes at codon 129 in the prion protein gene, indicating that this genetic subgroup (which is a different subgroup from that in which all cases of vCJD have so far occurred) is susceptible to vCJD infection

Individuals with this genotype may have a prolonged incubation period with subclinical infection and could cause secondary spread of vCJD by blood transfusion or surgery

Though it is inadvisable to overinterpret the data from only three positive cases in this study, it is perhaps surprising (given the relative prevalences of *PRNP* codon 129 genotypes in the general population) that both the positive cases analysed here were valine homozygotes. Though this may represent a chance finding, we should consider the possibility of differences in the peripheral pathogenesis of vCJD that depend on the *PRNP* codon 129 genotype. The patient who developed asymptomatic vCJD infection after red blood cell transfusion was a codon 129 heterozygote in whom both tonsil and appendix tissues were negative on staining for disease associated prion protein with identical methods as used in this study, though the spleen and lymph nodes gave positive results.[3] *PRNP* polymorphisms in sheep infected with scrapie also have a major influence on the incubation period and timing and distribution of disease associated prion protein in lymphoid tissues during the incubation period.[8]

A prolonged incubation period after infection with vCJD is likely to result in an asymptomatic carrier state (which cannot yet be identified), which represents a potential risk for horizontal transmission of vCJD infection by blood transfusion, blood products, or contaminated surgical instruments. These uncertainties further underline the need for continued surveillance of vCJD in the UK (including surveillance for subclinical or asymptomatic infection[9]), a requirement to continue to reduce the possibility of secondary iatrogenic transmission, and the inclusion of carrier states and susceptibility to vCJD infection in all *PRNP* codon 129 genotypes in future disease modelling.

Contributors: JWI (guarantor) and DAH were responsible for the prevalence study and the analysis of the results, including the selection of the cases for analysis, and drafted and modified the manuscript. MTB established the methods for DNA extraction and analysis, designed and executed the validation study, and drafted and modified the manuscript. KC and DH performed the DNA extraction on the test materials and in the validation study and modified the manuscript. MLeG, SL, DLR, and LMcC identified cases for the validation study and prepared the paraffin sections for DNA analysis and modified the manuscript.

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Competing interest: None declared.

Ethical approval: The prevalence study received approval from the South and West multi-centre research ethics committee (MREC reference 99/6/32) and for each of the centres included, appropriate local research ethics committee approval.

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Prescribing for RITA

And so it ends—a decade in the training grade. The last rites performed with a final RITA (record of in training assessment): I'm finally grown up, the authorities deem. In fact, my consultant job starts tomorrow.

After 10 years with it, do I have positive suggestions for postgraduate training in the NHS? Of course, dozens, most involving workforce, reorganisation, and resources. But, as in life, the best tonics are free. I vote for a fresh culture that values and grows people. It is remarkable that NHS doctors deliver their high quality service for no immediate tangible gain. More extraordinary is that this work receives not a trace of the positive feedback and moral incentive that would be critical to the health of any comparable organisation.

I worked for some time in a prestigious institution of a more advanced healthcare system. What made their people tick? True, they had impressive buildings, state of the art technology, and good salary prospects; but, really, I think they were primarily driven by an ethos that valued excellence and individuality—initiated, fostered, and rewarded it. Right down to the artwork that lined the corridors—oversized portraits of the previous month's star employees, proud pictures of "graduating" trainees, plaques of senior faculty.

A bit over the top perhaps, but preferable to the anonymous passage of generations of juniors through Britain's many worthy hospitals. In addition, attitudes of derision towards the less skilled and suspicion of those who seem too good or creative are all too common. The end result? Blunted clones coming off an assembly line: competent, yes; extraordinary, no. Tragic for individuals and undesirable for a healthcare system that confronts extraordinary problems.

There, I've had my shout. Tomorrow I step into a new world, recognising that to change it is to change myself. I will not forget my morning dose of free tonic.

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