mechanisms mediated by prion protein allows the human risks of bovine spongiform encephalopathy to be reassessed in similar terms. The likelihood that abnormal prion protein is the causative agent in all species provides a rationale for possible transmissibility between cows and humans: bovine spongiform encephalopathy and Creutzfeldt-Jakob disease are variants of the same entity. The undoubted transmission of prion disease between other species, under certain conditions, provides a precedent. Whether bovine spongiform encephalopathy prions, in practice, cause human disease depends on several other factors.

An important consideration relates to the aetiology of human prion disease in general: as most cases are not genetic or apparently infectively acquired, where do the abnormal prions originate? There may be unidentified somatic mutations in the prion gene in these cases, or they could be due to genetic or metabolic processes which have nothing to do with prions: neither mechanism need have any infective component. Alternatively, abnormal prions might come from an environmental source that has eluded detection because of its interaction with host prion gene polymorphisms and other factors. Although unlikely,²⁰ this explanation for some cases of prion disease cannot be discounted; it also follows that dietary exposure to abnormal prions due to bovine spongiform encephalopathy could have increased any such risk.

But, even if prion disease was caused by infection under certain, rare, circumstances, we may well have been protected from bovine spongiform encephalopathy for other reasons. Firstly, we may have been protected by the species barrier, which is due at least partly to interspecies variations in the prion gene.¹⁴ The differences between the encoded proteins may make the abnormal prions less able to convert the host's normal ones.¹⁴ The degree of similarity between bovine and human prion genes may therefore be an important determinant of the risk of infection. Secondly, the inefficiency of dietary spread of prion disease and the minimal infectivity of meat other than offal will both have greatly limited the dose of abnormal prions to which people were exposed.

In effect, bovine spongiform encephalopathy resulted from an accidental experiment on the dietary transmissibility of prion disease between sheep and cows. A subsequent experiment of this kind, involving humans, probably occurred in 1986-9 owing to produce contaminated with bovine spongi-

form encephalopathy entering the food chain during this period. The result of this experiment is awaited. Its interpretation will require careful epidemiological and neuropathological studies as we live through the "incubation period" over the next decades.¹²

Certainly no conclusive evidence exists to revise the consensus view that the chances of bovine spongiform encephalopathy causing human disease are extremely small^{1,2,3}; but neither can the possibility be dismissed. Meanwhile, clarifying the molecular biology will help to predict the outcome of the experiment and should eventually lead to treatments for prion disease regardless of its origin.

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- 1 Matthews WB. Bovine spongiform encephalopathy. *BMJ* 1990;300:1252-3.
- 2 Agriculture Committee. *Fifth report: bovine spongiform encephalopathy (BSE)*. London: HMSO, 1990.
- 3 BSE in perspective. *Lancet* 1990;335:1252-3.
- 4 Collee JG. Bovine spongiform encephalopathy. *Lancet* 1990;335:1252-3.
- 5 Kimberlin RH. Bovine spongiform encephalopathy. Taking stock of the issues. *Nature* 1990;345:763-4.
- 6 Harrison PJ, Roberts GW. Life, Jim, but not as we know it? Transmissible dementias and the prion protein. *Br J Psychiatry* 1991;158:457-70.
- 7 Will RG. The spongiform encephalopathies. *J Neurol Neurosurg Psychiatry* 1991;54:761-3.
- 8 Dealler SF, Lacey RW. Transmissible spongiform encephalopathies: the threat of BSE to man. *Food Microbiology* 1990;7:253-79.
- 9 Brown P, Gajdusek DC. Survival of scrapie virus after 3 years' interment. *Lancet* 1991;337:269-70.
- 10 Wilesmith JW, Ruan JBM, Atkinson MJ. Bovine spongiform encephalopathy: epidemiological studies on the origin. *Vet Rec* 1991;128:199-203.
- 11 Wyatt JM, Pearson GR, Smerdon TN, Gruffydd-Jones TJ, Wells GAM, Wilesmith JW. Naturally occurring scrapie-like spongiform encephalopathy in five domestic cats. *Vet Rec* 1991;129:233-6.
- 12 Prion disease - spongiform encephalopathies unveiled. *Lancet* 1990;336:21-2.
- 13 Hsiao K, Prusiner SB. Inherited human prion diseases. *Neurology* 1990;40:1820-7.
- 14 Prusiner SB. Molecular Biology of prion diseases. *Science* 1991;252:1515-22.
- 15 Lantos PL. From slow virus to prion: a review of transmissible spongiform encephalopathies. *Histopathology* 1992;20:1-11.
- 16 Hsiao K, Scott M, Foster D, Groth DF, DeArmond SJ, Prusiner SB. Spontaneous neurodegeneration in transgenic mice with mutant prion protein. *Science* 1990;250:1587-90.
- 17 Weissman C. A united theory of prion propagation. *Nature* 1991;352:679-83.
- 18 Brown P, Goldfarb LG, Gajdusek DC. The new biology of spongiform encephalopathy: infectious amyloidosis with a genetic twist. *Lancet* 1991;337:1019-22.
- 19 Collinge J, Palmer MS, Dryden AJ. Genetic predisposition to iatrogenic Creutzfeldt-Jakob disease. *Lancet* 1991;337:1441-2.
- 20 Palmer MS, Dryden AJ, Hughes JT, Collinge J. Homozygous prion protein genotype predisposes to sporadic Creutzfeldt-Jakob. *Nature* 1991;352:340-2.
- 21 Kingsbury DT. Genetic of response to slow virus (prion) infection. *Annu Rev Genet* 1990;24:115-32.
- 22 Baker HF, Poulter M, Crow TJ, Frith CD, Lofthouse R, Ridley RM, et al. Aminoacid polymorphism in human prion protein and age at death in inherited prion disease. *Lancet* 1991;337:1286.

Eusol

Still awaiting proper clinical trials

Eusol (an acronym for Edinburgh University solution of lime) is one of several hypochlorite solutions that have been widely used in the management of open wounds left to heal by secondary intention. As with many other traditional remedies their value remains scientifically unproved. Eusol consists of a chlorinated lime and boric acid solution containing 0.25% weight/volume of available chlorine with a pH between 7.5 and 8.5. Dakin's solution (introduced during the first world war) and Milton are similar but have a higher pH, whereas chloramine is an organic derivative with greater stability and a longer shelf life.¹⁻³

As disinfectants all these hypochlorites are effective for cleaning working surfaces and lavatories and for purifying water, but evidence is accumulating of their toxic effect

on healing tissues when used topically, which is causing controversy between traditionalists and experimentalists.^{4,7} Interestingly, Alexander Fleming suggested more than 70 years ago that the antimicrobial actions of antiseptics should be weighed against their potential toxic effects on tissues.⁸

The management of chronic wounds, healing by secondary intention, has been mainly delegated to nurses. After the publication of experimental studies showing that hypochlorite solutions may delay healing many informed nurses instigated a vendetta against Eusol, resulting in a virtual ban on its use in some districts. This experimental evidence would seem to have reinforced their personal experience, which had not previously been aired. Nursing journals have carried articles over the past five years consistently condemning

Eusol,⁶ but there is no evidence from clinical studies to support such a response.

The experimental evidence against Eusol, however, does give grounds for concern. In dilute concentrations it kills fibroblasts, neutrophils, and endothelial cells in tissue culture.⁹⁻¹² When applied to open wounds that are healing by secondary intention Eusol delays the appearance of hydroxyproline (the amino acid marker of wound collagen content) and prolongs the acute inflammatory response.¹³ Eusol damages mature granulation tissue after a single application.¹⁴

Eusol has no role in the treatment of open wounds that are clean and healing well with no signs of invasive infection. Cellulitis, lymphangitis, and other spreading infections need systemically administered antibiotics. Although infection is generally accepted to delay healing, there is no hard evidence that delays result from superficial colonisation of open wounds by commensals or even pathogens (with the possible exception of β haemolytic streptococci and pseudomonads).¹⁵⁻¹⁶ Evidence that antiseptics, or disinfectants like Eusol, reduce superficial bacterial counts is lacking; whether this is necessary for optimal healing is doubtful anyway. All antiseptics are rapidly inactivated by contact with tissues and body fluids, so that to have any lasting effect they would need to be continuously applied, which would be impractical.¹⁷

Do we need Eusol at all? A strong case can be made for its use in debriding burns or necrotic chronic wounds (such as venous ulcers or pressure sores), particularly before split thickness skin grafting. Anecdotally, such cleaning might reduce exudate and smell, thereby facilitating day to day management. There are other ways of cleaning necrotic ulcers, using simple surgical debridement together with occlusive or semiocclusive dressings, which are now prescribable in hospital and community based practice.¹⁸⁻²⁰

If Eusol was introduced today as a topical wound cleaner it would need a fight to attain a product licence. Whether it

should retain its place in the *British National Formulary* requires proper clinical trials. In dilute solution it might safely retain its effectiveness as an antimicrobial and wound cleaner, but only clinical trials will tell. All antiseptics have a toxic effect on healing tissues, but before their use is rejected completely the doubts raised by experimental studies on toxicity need clinical confirmation.

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- 1 Bloomfield SF, Sizer TJ. Eusol BPC and other hypochlorite formulations used in hospitals. *Pharmaceutical Journal* 1985;235:153-7.
- 2 Morgan DA. Chlorinated solutions: (E) useful or (e) useless? *Pharmaceutical Journal* 1989;239:219-20.
- 3 Thomas S. *Wound management and dressings*. London: Pharmaceutical Press, 1990:74-80.
- 4 Leaper DJ, Simpson RA. The effect of antiseptics and topical antimicrobials on wound healing. *J Antimicrob Chemother* 1986;17:135-7.
- 5 Leaper DJ, Cameron S, Lancaster J. Antiseptic solutions. *Nursing Mirror* 1987;April:30-4.
- 6 Brantley SK, St Arnold PA, Das SK. Antiseptic use in wound management. *Infections in Surgery* 1990;9:33-9.
- 7 Cunliffe WJ. Eusol—to use or not to use? *Dermatology in Practice* 1990;8:5-7.
- 8 Fleming A. The action of chemical and physiological antiseptics in a septic wound. *Br J Surg* 1919;7:99-129.
- 9 Lineaweaver W, McMorris S, Saucy D. Cellular and bacterial toxicities of topical antimicrobials. *Plast Reconstr Surg* 1985;75:394-6.
- 10 Cotter JL, Fader RC, Lilley C. Chemical parameters, antimicrobial activities and tissue toxicity of 0.1% sodium hypochlorite solutions. *Antimicrob Agents Chemother* 1985;28:118-22.
- 11 Deas J, Billings PJ, Brennan SS, Silver IA, Leaper DJ. The toxicity of commonly used antiseptics on fibroblasts in tissue culture. *Phlebology* 1986;1:205-9.
- 12 Kozol RA, Gillies C, Elgebaly SW. Effects of sodium hypochlorite (Dakin's solution) on cells of the wound module. *Arch Surg* 1988;123:420-3.
- 13 Brennan SS, Foster ME, Leaper DJ. Antiseptic toxicity in wounds healing by secondary intention. *J Hosp Infect* 1986;8:263-7.
- 14 Brennan SS, Leaper DJ. The effect of antiseptics on the healing wound: a study using the rabbit ear chamber. *Br J Surg* 1985;72:780-2.
- 15 Eriksson G, Eklund AE, Liden S, Zetterquist S. Comparison of different treatments of venous leg ulcers: a controlled study using stereophotogrammetry. *Current Therapeutic Research* 1984;35:678-84.
- 16 Hutchinson JJ, Lawrence JC. Wound infection under occlusive dressings. *J Hosp Infect* 1991;17:83-94.
- 17 Gardener JF, Peel MM. *Introduction to sterilisation and disinfection*. Edinburgh: Churchill Livingstone, 1986.
- 18 Local applications to wounds. I. Cleaners, antibacterials, debriders. *Drug Ther Bull* 1991;29:93-5.
- 19 Local applications to wounds. II. Dressings for wounds and ulcers. *Drug Ther Bull* 1991;29:97-100.
- 20 Leaper DJ, ed. *International symposium on wound management*. Bussum, Netherlands: Medicom, 1991.

Taking infants' temperatures

Forget the axilla—the rectum is better

Deciding what to do when an infant seems unwell may be difficult for both parents and doctors. Parents measure sick children's temperatures to help them decide whether to give an antipyretic drug or call the doctor, while the doctor's main decision is whether to treat the child at home or to refer to hospital. Recent publicity given to the possible role of high temperature in the sudden infant death syndrome will probably increase parental anxiety about measuring children's temperature.

Measuring the temperature is an important part of assessing an unwell infant.¹ Subjective assessments of the presence or absence of fever are unreliable,² and a raised core temperature is more likely to indicate a serious problem in an infant who does not feel hot.

But where should the temperature be taken? In continental Europe parents and health professionals routinely take infants' temperatures rectally. In Britain parents favour the axilla; this is in line with current British health education³ and, in general, with the advice of midwives and health visitors. In a survey of general practitioners' attitudes published in this week's journal only half the general practitioners questioned would consider taking a rectal

temperature in infants, while a substantial minority believed that there was no place for taking rectal temperatures in general practice (p 961).⁴

Some doctors have argued against measuring the rectal temperature because of the risks of thermometer breakage,⁵ rectal injury,⁶ and cross infection.⁷ These risks have been exaggerated. Reviewing the literature Morley and colleagues estimate the risk of rectal perforation by a thermometer at less than one in two million.⁸ Such minute risks are far outweighed by the superior reliability, speed, and convenience of rectal temperature measurement.

Several studies have shown the unreliability of axillary temperatures in children.⁸⁻¹¹ Using conventional mercury in glass thermometers placed in the axilla for eight minutes, Kresch found a sensitivity for fever of only 33%,⁹ while Weiss *et al*, using electronic thermometers, concluded that axillary temperatures were unsuitable for use as a screening test because of poor sensitivity.¹⁰ In a study of 937 infants under 6 months Morley and colleagues found axillary measurement to have a false negative rate for fever of 75% in the home and 27% in hospital⁸—both unacceptably high. Axillary and rectal measurements were found to differ inconsistently by up to