Scrapie was probably introduced into Iceland in 1878 by an imported ram of the Oxford-Down breed that was brought to a farm in the mid-north of Iceland. Its descendants were used widely for breeding in the adjoining area and, a few years later, scrapie was detected in this region. At the beginning of the 20th century, scrapie had spread to a considerable part of the mid-north and has remained endemic in this area ever since (Fig. 1; Pálsson, 1979). During a campaign begun in the 1940s to eradicate lentiviral diseases of sheep and paratuberculosis of sheep and cattle, the country was divided into 30 quarantine areas by fences and natural boundaries such as rivers and glaciers. The number of these quarantine areas was later increased to 38 when plans to control, and subsequently eradicate, scrapie were implemented. During this campaign, all sheep in the original endemic scrapie areas were culled and restocked with lambs from scrapie-free areas. However, scrapie recurred on 33 farms. Nine of these recurrences occurred 14–21 years after culling, apparently as the result of environmental contamination, but outside entry could not always be absolutely excluded. Of special interest was one farm with a small, completely self-contained flock where scrapie recurred 18 years after culling, 2 years after some lambs had been housed in an old sheep-house that had never been disinfected. Epidemiological investigation established with near certitude that the disease had not been introduced from the outside and it is concluded that the agent may have persisted in the old sheep-house for at least 16 years.

One of us (S.S.) travels frequently around the countryside to inspect sheep and to increase the awareness of both farmers and district veterinarians about the disease, and also attends the main sheep gatherings in the autumn, when the sheep are driven from summer pastures in the mountains to common corrals on the lowland. In addition to brain samples from suspect sheep and fallen stock, random samples are collected on average every 3 years from slaughterhouses serving both scrapie-endemic and scrapie-free quarantine regions, yielding approximately 10 000 samples per year. At the Institute for Experimental Pathology, the brains are examined histologically for spongiform changes and, in the last 7 years, also immunostained to detect the pathognomonic affected flocks, banning trade with live sheep from affected and suspected flocks, disinfection of premises and restocking with lambs from healthy flocks. However, scrapie continued to spread, at least in part because of non-compliance (P. A. Pálsson, personal communication). In 1978 and again in 1986, revised plans were implemented. The main features of these plans were: (i) slaughter of all sheep in scrapie-affected flocks and sometimes also of healthy flocks considered to be at risk; (ii) destruction of hay, disinfection of sheep-houses, barns and equipment and, in some instances, burning of old decrepit sheep-houses and replacement by new buildings; (iii) ban on the movement of sheep, hay and equipment from scrapie-affected farms between and within quarantine areas; (iv) restocking after a minimum of 2 years with lambs from scrapie-free areas remote from affected quarantine zones; and (v) continuous health control of new flocks to detect possible recurrence.

In 1957, a plan was initiated to halt the spread of scrapie that consisted of compulsory reporting, culling of heavily
presence of proteinase-resistant prion protein (PrPSc). More recently, ELISA has also been used for screening.

For histological examination, three blocks were cut from the medulla oblongata and embedded in Tissue-Tek (Sakura); sections were cut at 5 μm and stained with haematoxylin/eosin (HE). Based on a 40 year experience, we have always found that lesions are most severe in the medulla oblongata and that the initial vacuolization occurs in the dorsalis nucleus of the vagus nerve (Thorgeirsdottir et al., 2002). For immunostaining, formaldehyde-fixed, Tissue-Tek-embedded blocks were cut at 5 μm and, after pretreatment, were stained with a mAb to PrPSc, which defines a conserved epitope on the ruminant prion protein (O'Rourke et al., 1998), and visualized with a secondary peroxidase-labelled antibody amplified with peroxidase–anti-peroxidase complex and diaminobenzidine as substrate. The results of immunostaining confirmed our diagnosis of scrapie by conventional HE staining, and we did not find a significant difference between conventional histological examination, immunohistochemical staining and Western blotting in detecting subclinical infection (Thorgeirsdottir et al., 2002).

We analysed records kept at the Institute from 1978 to 2004. Recurrences were detected on 33 farms, all in quarantine zones where scrapie-affected farms were most numerous: 16 were in the original endemic area, four were in the north-eastern part of the country, 12 were in the east and one was in the south (Fig. 2). Recurrences were occasionally detected 1–3 years after restocking, but most frequently after 4–7 years. However, on nine farms, scrapie recurred as late as 12–19 years after restocking, i.e. 14–21 years after culling.

In most of the nine farms with late recurrences, we could not find any evidence for the introduction of scrapie from the outside, but the possibility of grazing on common pastures in the interior highlands or participation at autumn sheep gatherings could not always be excluded with certainty.

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**Fig. 1.** Scrapie was probably introduced into Iceland in 1878 from an imported ram (●). By the beginning of the 20th century, it had spread widely in the mid-northern part of the country (shown in grey) and, at the height of the epidemic in mid-century, it had spread to all except 13 of 38 quarantine areas (shown in black).

**Fig. 2.** Scrapie recurrences (●) during the period 1978–2004. All farms were within areas with the highest density of scrapie farms (shown in grey), based on cumulative incidence from 1953 to 1999 (Sigurdarson, 2000). Quarantine areas are bounded by solid lines and glaciers are indicated by G.
However, even these low-risk activities could be eliminated on one farm where scrapie had occurred in 1982 and recurring 18 years later in 2000. The entire flock had been culled in 1982 and restocking was done with healthy lambs from a scrapie-free area 3 years later in 1985. The flock was small (68 sheep) and had no contact with outside sheep. The farmer had bred his flock from lambs obtained from scrapie-free regions, for which the farmer had kept detailed records. The only other appearance of scrapie in this quarantine zone during the period 1982–2004 occurred in 1991 in one flock 35 km distant, which had had no communication with the studied flock and was culled shortly after detection of scrapie. The flock was self-contained, i.e. animals grazed in the spring on home pastures and during the summer in the mountain above the farm, and were not driven to common pastures in the interior. In addition to culling of the entire flock in 1982, the sheep-houses had been burnt and replaced by new buildings located and fenced off at some distance from the farmhouse, except for a single small sheep-house close to the farmhouse, which was old and impossible to disinfect properly.

The entire new flock was kept in the new building until 1998 (i.e. 16 years after culling of the old flock), when the farmer moved a few 4–5-month-old lambs selected for breeding into the old sheep-house. Two years later, one of these animals developed clinical scrapie, confirmed by neuropathological examination. Again, the entire flock was killed and subjected to neuropathological and immunostaining for PrPSc of lymphoid tissue and medulla oblongata of the asymptomatic sheep. Subclinical infection was detected (almost exclusively in the lymphoid tissues) in 58% of the flock.

Icelandic sheep are housed indoors for 6–8 months of the year, where they are especially exposed to infection either through direct contact or from contamination of hay, water and of the sheep-houses. Infection through feed concentrates during the period of observation can be excluded because of strictly enforced bans on both the importation of meat-and-bone meal and its use from any source in ruminant feed since 1978. We also looked into the question of whether wild rodents could act as vectors. Neuropathological study of a limited number of long-tailed wood mice (Apodemus sylvaticus) on farms where scrapie had been endemic for decades failed to disclose a single positive animal (G. Georgsson, unpublished results).

Given that no epidemiological investigation, particularly one with a historical basis, can be guaranteed to be both 100% complete and accurate, we believe that the facts surrounding the recurrence of scrapie in the flock in question, including its appearance 3 years after the only identified exposure to contamination (consistent with innumerable experimental field observations), can be explained most plausibly by contamination from scrapie agent that had persisted inside the sheep-house for 16 years.

The similarity of sheep genotypes (in particular, the high-risk genotype VRQ) in scrapie-free quarantine areas and scrapie-affected quarantine areas supports our hypothesis that scrapie-free status results exclusively from an absence of exposure to the scrapie agent (Thorgeirsdottir et al., 1999). The occurrence of high-risk genotypes in scrapie-free quarantine areas makes it highly unlikely that scrapie could have remained subclinical in these areas for more than a century. Our finding of recurrences exclusively in quarantine areas where scrapie-affected farms have been most numerous further emphasizes the effect of a contaminated environment (Fig. 2).

Recently, it has been shown that the infectious agent binds strongly to several minerals in the soil (Johnson et al., 2006). Support for the durability of infectivity comes from our earlier field experience showing that the scrapie agent can persist for at least 3 years in the environment (Pálsson, 1979) and from experiments showing residual infectivity in earth contaminated by scrapie hamster brain after 3 years interment (Brown & Gajdusek, 1991) or by decayed carcasses of mule deer with chronic wasting disease after a period of more than 2 years (Miller et al., 2004).

The long-term persistence of the infectious agent in the environment highlights the difficulties in eradicating scrapie of sheep and sounds a serious warning about the risk of disposing of sheep carcasses from scrapie-affected flocks by burial. The high incidence (58%) of subclinical infection in a flock having only a single symptomatic animal is another concern, and may be a more widespread phenomenon than is appreciated currently [we have also detected subclinical infection by immunostaining and Western blotting of brain samples from 41% of apparently healthy sheep in a different scrapie-affected flock (Thorgeirsdottir et al., 2002)].

Scrapie is not known to infect humans directly; however, it is highly likely that it did infect cattle (as BSE), which in turn infected humans (variant Creutzfeldt–Jakob disease). Such species-barrier crossings could be dangerous, should it be discovered that BSE has been transmitted to and maintained in genetically diverse European sheep breeds (Asante et al., 2002). At least one goat (in France) has contracted BSE in the field (Elloit et al., 2005) and it has recently been shown that BSE can also be transmitted naturally to healthy sheep from sheep infected experimentally with BSE (Bellworthy et al., 2005). It is to be expected that the agent of BSE, which shows chemical and physical resistance equal to or greater than that of any other tested strain of TSE (Taylor et al., 1994; Schreuder et al., 1998; Cardone et al., 2006), may persist for at least as long in the environment as the scrapie agent. The burial of thousands of sheep and cattle during a recent foot-and-mouth disease outbreak in the UK, and possible illegal burial of BSE cattle, is thus of concern for public health.

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References


