because there's so much glutamate floating around the cell that it's tricky to pinpoint proteins that act on it, says Caron.

Edwards's team actually worked with this long-sought protein, now dubbed VGLUT1, for a few years before realizing its true identity as a glutamate transporter. Other researchers had pegged it as a phosphate transporter. But there were hints that it had greater powers: A mutation of a closely related protein in the worm *Caenorhabditis elegans* appeared to disrupt glutamate transmission. And mutations of another related protein in humans cause acid to build up in cellular bubbles called lysosomes. The UCSF team originally suspected that the protein might, through its ability to transfer phosphate, modulate some other protein's ability to pack glutamate into vesicles. They tracked the protein down to vesicle walls, suggesting that it was a key player in hustling chemicals in and out of these packages. As evidence mounted that the protein was more than a phosphate transporter, "we had to change our thinking," recalls Edwards.

To test whether VGLUT1 could transport glutamate into vesicles itself, Edwards's team, which includes Elizabeth Bellocchio, Richard Reimer, and Robert Fremeau Jr., inserted the gene that codes for the protein into some cells of a standard cell line. They then caused the cells to build mock vesicles and tested how much glutamate got into these chambers. Cell lines that contained VGLUT1 packed two to four times as much glutamate into their model vesicles as did those without. "I think their characterization is very convincing," says Caron.

Still, there are a few loose ends. Glutamate buzzes throughout the brain, but VGLUT1 is much more localized. Even so, says Edwards, this doesn't disqualify it as the long-sought glutamate transporter: Another, closely related protein shows up in the areas of the brain where VGLUT1 is absent. He thinks the two carry out similar functions but are distributed in different parts of the brain.

Now that they've identified the glutamate vesicular transporter, the UCSF researchers hope to figure out how it works. True transporters actively escort neurotransmitters into a vesicle, pulling them uphill against the gradient between the tightly packed neurotransmitters inside and the low concentration outside the vesicle. It's a slow process, but it can pack in more chemicals than the alternative, a channel. Channels essentially open up part of the vesicle wall, enabling chemicals to surge in, attracted by a charge or pH gradient. Strangely, the glutamate transporter appears to have properties of both: It packs glutamate into vesicles both extremely tightly and extremely quickly. "We're thinking about all sorts of models right now," says Edwards. **–LAURA HELMUTH**

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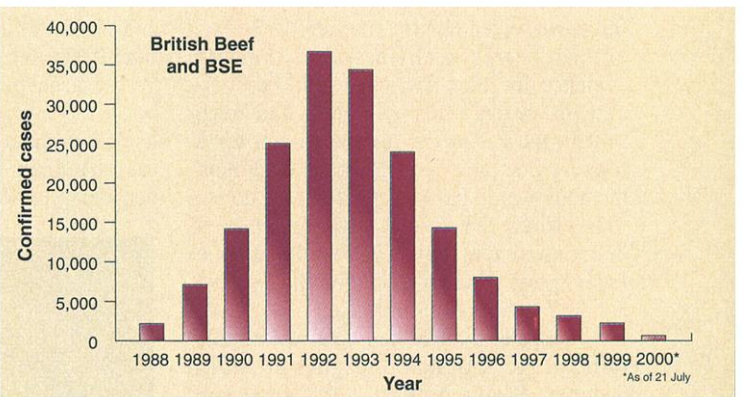
EMERGING DISEASES

Hunt for Mad Cow in Sheep Reassuring

Experts on brain-riddling spongiform diseases have grown steadily more uneasy over signs that so-called mad cow disease, linked to a lethal human illness, may be lurking in sheep. Not only would that open up a new front in the battle to purge bovine spongiform encephalopathy (BSE) from livestock, but it would also suggest that far more people—at least those who eat lamb, anyway—are at risk of contracting the human killer, variant Creutzfeldt-Jakob disease (vCJD). A study in the 10 August issue of *Nature* now offers evidence that BSE is not rampant in sheep after all, although scientists are far from ready to let their guard down.

Spongiform diseases rob their victims—be they sheep, cattle, or people—of their balance, their minds, and inexorably their lives. As of 30 June, 75 confirmed or probable vCJD cases had been diagnosed in the United Kingdom, according to a study led by the U.K.'s National CJD Surveillance Unit in Edinburgh that appeared in the 5 August issue of *The Lancet*. vCJD cases have increased an average of 23% each year since 1994, and projections based on average incubation times of the disease have raised the specter of tens or even hundreds of thousands of deaths in the coming years from exposure to BSE.



Over the hump? Researchers did not uncover a significant jump in reported scrapie cases in concert with the BSE boom in cattle *(above)*, suggesting that sheep did not experience a BSE epidemic.

With BSE in British cattle on the wane (see chart), some experts now worry that BSE might be circulating in sheep, where it could be masked by scrapie, a related disease with very similar symptoms (*Science*, 17 March, p. 1906). Although there is no evidence to date that sheep can become infected naturally with BSE—nor that scrapie itself is transmitted to humans—sheep experimentally infected with BSE develop scrapielike symptoms. This raises fears that if a BSE epidemic occurred in sheep, it might be confused with scrapie. Indeed, there has been speculation that BSE may be to blame for a scrapielike illness recently reported in some sheep in Vermont.

Like BSE, scrapie, which has flourished in British flocks for more than 250 years, is thought to be caused by infectious prion proteins. If BSE jumped into sheep from cattle, there might be a spike in the incidence of reported "scrapielike" cases during the height of the BSE epidemic in cattle between 1990 and 1995. To investigate this possibility, a U.K. team from the Institute for Animal Health in Compton, the Veterinary Laboratories Agency in Surrey, and the University of Oxford analyzed scrapie incidence between 1962 and 1998, using data from an anonymous mail survey of 11,554 sheep farms. Their numbers show that scrapie incidence has risen slowly, but there is no noticeable jump in scrapie cases before, during, or after the height of the cattle BSE epidemic in the early 1990s, when up to 36,000 cases of mad cow disease were reported each year. The authors interpret this to mean that the BSE epidemic in cattle did not lead to a comparable BSE epidemic in sheep. The data also show that farms raising both sheep and cattle did not run a higher scrapie risk, which might have been expected if many BSE cases were masquerading as scrapie.

Although the survey doesn't eliminate the nightmarish possibility of BSE in sheep, "one can at least be confident that there has not been an epidemic in sheep equivalent to that in cattle," says epidemiologist Peter Smith of the London School of Hygiene & Tropical Medicine, acting director of the U.K.'s Spongiform Encephalopathy Advisory Committee. The authors note that although their analysis was fine enough to detect a doubling of scrapie cases over the baseline incidence, a smaller blip, representing a smaller scale epidemic, may have gone unnoticed. Direct biochemical tests for BSE infection in cattle are now in use in Europe, but tests to distinguish BSE from scrapie are not yet available—leaving indirect studies as the only way to gauge infection rates. Thus, says Smith, "we cannot exclude the possibility that BSE was in sheep at a low level."

Although the new findings are comforting, researchers plan to keep a wary eye on sheep. As they know all too well, the history of the BSE epidemic and the emergence of vCJD illustrate the high price of complacency.

–MICHAEL BALTER