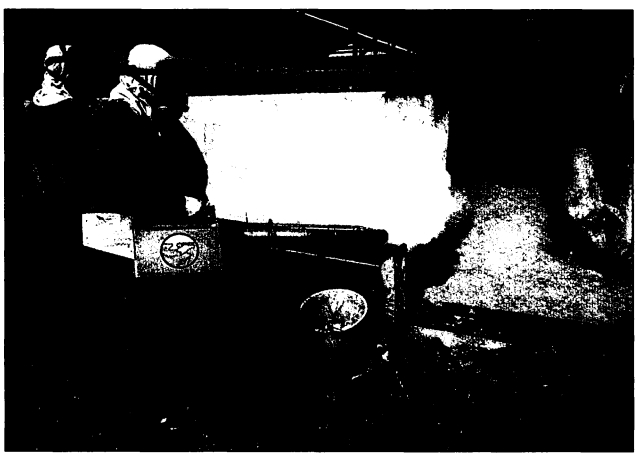
though some scientists say that the possibility of theft should not be discounted, most express confidence that their labs are secure. "Barring a SWAT team or someone with bazookas, I think we actually have a pretty safe situation for the cultures," says Keim.

–JOSHUA GEWOLB

BIOTERRORISM

Congress Weighs Select Agent Update

U.S. researchers may soon be haggling with the government over which viruses, bacteria, and biological toxins should be tightly regulated. Congress this week was expected to begin debating a proposal to impose new security requirements on laboratories working with these pathogens and to update the government's list of about 40 regulated "select agents." But experts say that it is unclear whether the core list—which the United States hopes other countries will adopt—should expand or shrink.



Deadly addition. The Nipah virus would be a candidate for a new list of regulated bioagents.

The legislation, to be introduced by Senators Edward Kennedy (D–MA) and Bill Frist (R–TN), is the latest congressional response to the anthrax mail attacks that have killed four people in the United States. It follows a newly imposed ban on the possession of such agents by scientists from so-called terrorist nations. The latest proposal—some version of which is expected to become law within weeks—is intended to boost government spending on vaccines and strengthen the nation's defenses against bioterrorism. But it would also increase federal oversight by requiring greater lab security and registration of select agent collections and certain types of research equipment.

The debate over which agents to include would be triggered by language ordering the Department of Health and Human Services (HHS) to revise its select agent list every 2 years. Although periodic review is a good idea, say experts, the exercise is likely to be dogged by technical disagreements. "Coming up with the first list wasn't easy," recalls Janet Shoemaker of the American Society for Microbiology, which in 1996 helped the Centers for Disease Control and Prevention (CDC) in Atlanta evaluate hundreds of candidates to comply with a law that requires registration for labs that ship or receive potential bioweapons. "No two people ever agree on what should be on these lists," says David Franz, a former commander of the U.S. Army Medical Research Institute of Infectious Diseases in Fort Detrick, Maryland.

Researchers involved in the evaluation say there was consensus on listing highly lethal organisms that are relatively easy to turn into weapons, such as smallpox, anthrax, plague, tularemia, and a number of viral hemorrhagic fevers. But other agents sparked debate. A draft list generated nearly 70 letters, and CDC responded by dropping agents such as Western equine encephalitis virus and a bacterium called *Chlamydia psittaci* and adding equine morbillivirus and a fungus called *Coccidioides immitis*. The current list contains 13 viruses or virus groups, nine bacteria, three rickettsiae species, a fungus, and 12 types of toxins (*Science*, 2 November, p. 971).

One challenge for the CDC will be squaring its list with similar compilations by other bioweapons experts. Western equine encephalitis, for instance, is still listed as a potential threat by another CDC analysis. A loose consortium of 34 countries that works to limit the export of biothreats, called the Australia group, includes food- and waterborne diseases, such as salmonella and cholera, that are absent from the CDC list. The North Atlantic Treaty Organization, meanwhile, has its own list that includes dengue and influenza. These agents are not usually fatal, but they can bring an army to its knees. There are also extensive lists of potential agricultural threats, but Congress appears content to leave their regulation in the hands of the U.S. Department of Agriculture.

Another problem is that the world doesn't stand still. "We learn new information all the time," says Robert Shope, a virologist at the University of Texas Medical Branch in Galveston. In 1999, for instance, the newly identified Nipah virus killed more than 100 people in Malaysia and decimated its pork industry (*Science*, 16 April 1999, p. 407).

Future listmakers must balance the benefits of being comprehensive against the costs of burdening law enforcement and research efforts, say bioterror experts. One option is to split the list into two classes, with the riskier agents—such as anthrax—subject to more stringent regulation. Administration officials have also floated the idea of setting up a new enforcement office within HHS to police microbe research, because CDC, a public health agency, has traditionally resisted that role. "We are not a regulatory agency and don't profess any expertise or much experience in that," CDC head Jeffrey Koplan told reporters last week.

The scope of the list will determine the number of researchers and laboratories affected. About 250 U.S. university, government, and private labs are registered to handle the agents on the current list. But CDC officials expect that number to grow because of a processing backlog and because many labs have been tardy in filing their paperwork. Scientists in other countries could be subject to similar systems if their governments follow the U.S. lead, and the United Kingdom has already introduced legislation to criminalize possession of certain bioagents. The Bush Administration supports that approach as a substitute for the proposed Biological and Toxin Weapons Convention protocol, now stalled.

–MARTIN ENSERINK AND DAVID MALAKOFF

GENES AND DISEASE

Immune Gene Linked To vCJD Susceptibility

Researchers have found that a common variation of an immune system gene may offer some protection against variant Creutzfeldt-Jakob disease (vCJD)—the fatal neurodegenerative disease linked to eating cattle infected with "mad cow disease." The new finding—the second genetic factor discovered so far that influences susceptibility to the disease—may help to identify high-risk individuals and provide some clues to the modus operandi of this mysterious, incurable malady.

Most researchers believe that vCJD and similar diseases in humans and animals are caused in whole or in part by aberrant proteins called prions, which are misfolded versions of a normal cellular protein called PrP. Infection with vCJD appears to be caused by ingesting prions in contaminated meat.

Researchers have long known that an individual's genetic makeup influences susceptibility to the disease. One genetic factor exerts a particularly powerful influence: So far, every one of the more than 100 people diagnosed with vCJD in the United Kingdom has both copies of the *PrP* gene producing the

CREDIT: VINCENT THIAN/AP

Prion proof? A common genetic factor may give protection against the human form of mad cow disease.

amino acid methionine at position 129. And two papers published earlier this year in the *Proceedings of the National Academy of Sciences* showed that at least seven other genes affect susceptibility to prions in mice. "We knew that there must be a whole range of other genes" that determine prion disease risk in humans, says neuropathologist James Ironside of the National CJD Surveillance Unit in Edinburgh, U.K.

Now, one of those genes may have been identified: A team led by neurologist John Collinge of Imperial College, London, reports in this week's issue of *Nature* that more than 80% of vCJD victims lack a fairly common version of an immune system protein called human leukocyte antigen (HLA), which helps the immune system recognize infectious agents.

The HLA proteins, which vary from individual to individual depending on their genetic makeup, come in many different forms. One form, called HLA-DQ7, was found in 70 out of 197 normal control individuals, or 35.5%. But Collinge's team found that of 50 vCJD patients studied, only 6, or 12%, had the DQ7 variety of HLA. The researchers conclude that DQ7 somehow protects individuals from vCJD. One possibility would be that DQ7 helps the immune system fight off prions. But DQ7 could play another role: Recent studies suggest that prions must travel through immune system organs such as the lymph nodes and the spleen to get from the gut to the brain. If HLAs are involved in this transport, for example by binding to the prions—and if DQ7 is less efficient in this role—this could also explain the results.

"We know that lymphoid organs are crucially important," says neuropathologist Adriano Aguzzi of the University of Zürich. "So it hardly comes as a surprise that the second [genetic factor] to be discovered" is an immune system component. But Aguzzi, as well as the paper's authors, caution that DQ7 may play only an indirect role: It could just be closely linked to other genes that are more directly controlling susceptibility to vCJD. "Time, additional patients, and additional genetic studies will be needed to settle this issue," Aguzzi says. **–MICHAEL BALTER**

CREDITS: (TOP TO BOTTOM) JOHN REDMAN/AP; FERNANDO ARMATI

GENES AND DISEASE

Genetic Change Wards Off Malaria

Researchers have determined that a genetic alteration can provide almost complete protection against malaria, which in Africa kills 3000 children each day. The alteration produces a form of the oxygen-transport molecule called hemoglobin C. Another version of hemoglobin, hemoglobin S, also helps ward off malaria, but that protection comes with a steep cost: People who inherit two copies of the hemoglobin S gene develop severe sickle cell anemia. By contrast, hemoglobin C seems to have no adverse effects. Understanding how hemoglobin C works could help guide the development of vaccines and drugs, says Thomas Wellems, a malaria researcher at the National Institute of Allergy and Infectious Diseases in Bethesda, Maryland.

Earlier work had hinted at a protective role for hemoglobin C. Now, in the 15 November issue of *Nature*, malaria researchers Mario Coluzzi and David Modiano of the University of Rome La Sapienza and their colleagues demonstrate its value. The work "shows that hemoglobin C is much more important than hemoglobin S," comments Francisco Ayala, a population and evolutionary geneticist at the University of California, Irvine, who has studied the origins of this disease.

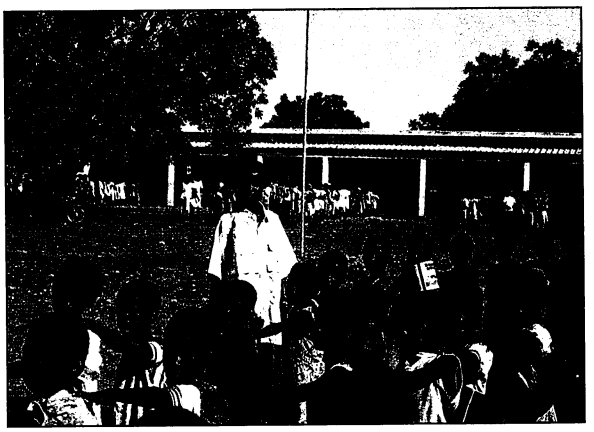
Modiano and Coluzzi and their colleagues pinned down hemoglobin C's role by studying 4348 Mossi children in Burkina Faso, West Africa. They took blood samples from 3500 healthy children, 359 children with severe malaria, and 476 children who had less serious cases. The team then determined which versions, or alleles, of the hemoglobin gene were present in each sample.

They found a striking difference between healthy and sick children in the ratio of those with two copies of the typical hemoglobin allele, A, to those with two hemoglobin C genes, or to those with one of each. Few sick children had one or two hemoglobin C alleles, suggesting that the allele is beneficial. Indeed, the researchers found just one malaria patient who had two copies of the hemoglobin C gene, whereas 14 would be expected had there been no protective effect. Moreover, extenuating circumstances may have increased that child's vulnerability to malaria, says Coluzzi. Having a double dose of hemoglobin C "is almost complete protection," Coluzzi explains.

Coluzzi cautions that these results won't translate quickly into better treatments. But they do speak to how these hemoglobin genes evolved in African populations—a history that is quite intriguing, says Clive Shiff, a malaria researcher at Johns Hopkins School of Medicine in Baltimore. For example, if two copies of hemoglobin C are as beneficial as these data show, "one would expect hemoglobin C's [prevalence] in the population to change very fast," he explains. If natural selection were at work—and if there were no hidden fitness costs to having this hemoglobin—many more people with hemoglobin C would survive to reproduce than would those with other alleles. Thus, their descendents should quickly predominate. Yet the other hemoglobin alleles seem to be persisting through time, Shiff points outs.

Coluzzi attributes this phenomenon to the availability of malaria treatments. He estimates that the genetic mutation that created hemoglobin C occurred only about 1000 years ago in the Mossi and that the allele is now spreading rapidly among that group. But it would replace the other alleles only "in the absence of drugs," he explains, because drugs enable those with malaria to survive and reproduce.

To find out more about hemoglobin's place in humankind's fight against malaria, Coluzzi's team is keeping track of the children with this allele to see if their hemoglobin continues to keep them healthy. **–ELIZABETH PENNISI**



Good genes. Some West African children have antimalaria hemoglobin.