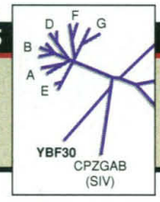


CREUTZFELDT-JAKOB DISEASE

Britain Hunts Down CJD Epidemic In Removed Appendixes

LONDON—Ever since the first deaths in 1995 from a new form of brain disorder thought to result from eating the meat of cattle infected with mad cow disease, one critical question has remained unanswered: How many cases are likely to show up beyond the 27 diagnosed so far? Given the long latency period for the disease—perhaps 10 years or more—it is hard to tell whether the country is facing a silent epidemic or just a smattering of cases. Last week, the British government announced that it is about to launch a novel study to try to find out.

PA NEWS

The big question. U.K. chief medical officer Kenneth Calman has approved a survey of 1000 organs for nvCJD.

It will examine hundreds of stored tonsils and appendixes, removed during surgery in the past several years, for signs of the rogue prion proteins that have been linked to the brain disorder, known as new-variant Creutzfeldt-Jakob disease (nvCJD). Kenneth Calman, the government's chief medical officer, who announced the study at a press briefing last week, said it "is only sensible to explore" what he called "the biggest question" surrounding the disease. But the study, which is still at the planning stage, will confront an ethical minefield over such questions as whether to tell healthy patients whose organs test positive.

The study was prompted by the case of Tony Barrett, a 45-year-old coast guard from southwest England, who died of nvCJD in June. According to a paper in the 29 August issue of *The Lancet*, Barrett developed the first symptoms of the disease—numbness of his face and right hand—in May 1996. Eight months earlier, he had had his appendix removed at a local hospital. "I saw that Mr. Barrett had an appendectomy in September 1995, and we felt some of the lymph nodes contained in the organ could reflect traces of the disease," says David Hilton, a neuropathologist at Derriford Hospital in Plymouth. "Tests revealed that we were correct, and these were corroborated at the National CJD Surveillance Unit in Edinburgh."

It was the first demonstration that nvCJD can be detected before symptoms appear, says James Ironside of the National CJD Surveillance Unit, a co-author of the *Lancet* paper. John Collinge of London's Imperial College, a member of the government's spongiform encephalopathy advisory committee (SEAC) who has developed tests for the disease in the tonsils, says the discovery of prions in the appendix was not surprising, however. Earlier studies on scrapie, the sheep equivalent of CJD, revealed that lymphoid tissue, such as in the gut, tonsils, and spleen, were infected with prions a third of the way through the incubation period and long before symptoms developed. From the lymphoid system, the prion protein is thought to pass into the nervous system and then the brain. Researchers do not know, however, at what stage lymphoid tissue becomes involved during the incubation period of nvCJD.

> **The new finding "provides us with an opportunity which it is only sensible to explore."**
>
> **—Kenneth Calman**

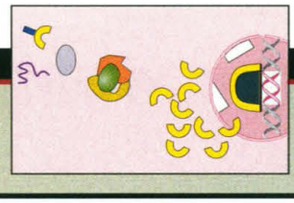
The Barrett case suggests that it occurs early enough to justify a broad study to look for silent infections. The government plans to test more than 1000 of the 800,000 samples of tonsil and 45,000 samples of appendix removed and stored each year. Comparison of tissue removed before and at the height of the BSE epidemic in the late 1980s may provide a rough indication of the extent to which the population harbors nvCJD prion proteins. But the size of the study may be a problem. If just one in 1000 cases proves positive, in a population of 50 million, that would imply that 50,000 people are infected. "Interpretation of the studies will require considerable caution," says Calman.

The Medical Research Council is considering a proposal by Collinge for a study of tonsils, while Ironside would coordinate the appendix studies through the Department of Health. Ironside says the study would use antibodies to detect the prion proteins in the stored tissues: "The [antibody] staining technique is a straightforward method, and with appropriate approval and resources we could start in the next few months."

Government officials and their advisers have not yet worked out the ethical rules that will govern the testing program, however. One option is for a scheme similar to one used in Britain for HIV testing of donated blood, where unlinked, anonymous samples are examined. It is impossible under this protocol to trace the person donating the sample. "If you want to have an HIV test, you cannot get the result from this program," says a Department of Health official. Britain's large bank of surgical tissue samples stored at hospitals around the country, which contains material more than 50 years old, is often used anonymously in new histological studies for the analysis of cancer, for example.

If the study uses tissue that is not anonymous, it will have to deal with the issue of whether to tell patients if researchers do detect prions in their removed organs. There is currently no treatment for nvCJD. Although SEAC is still considering what advice to give the government, Calman says the Department of Health is looking at the best way to carry out anonymous studies on the appendixes and tonsils.

Aside from the ethics of the testing pro-



gram, the discovery that prions can lurk in organs long before people show signs of disease has another alarming implication: that surgical instruments used on those people could pass on the disease. It has long been recognized that the infectious agent responsible for the classical form of CJD can be transmitted that way. In one case, brain electrodes that had been sterilized passed the infection from one patient to a second. They were sterilized again but passed the disease on to a third patient. SEAC says spread by surgical instruments is an "unlikely mode of transmission" after an appendectomy, particularly as the scalpel blade is thrown away. But Calman has set up a new expert group to carry out further assessment of procedures used to decontaminate instruments which "will start shortly." —NIGEL WILLIAMS

PLANETARY SCIENCE

Lunar Prospector Probes Moon's Core Mysteries

Most planetary scientists suspect that far beneath the cold craters and dusty seas of the moon lies an important clue to its fiery past—a dense core. Now the modestly outfitted Lunar Prospector spacecraft has gathered gravitational and magnetic data that offer support to those suspicions and hint at the size of this small metallic nugget. The new findings, presented with other Prospector results on page 1475 of this issue, fit with a theory that the core is the remnant of a violent crash between the infant Earth and a Mars-sized body that spawned the moon 4.5 billion years ago.

The discoveries lengthen a string of successes by NASA's desk-sized $63 million robot, launched in January, which spotted signs of frozen water at the moon's poles last winter (*Science,* 13 March, p. 1628). Skimming just 100 kilometers above the moon's surface, Prospector has put together detailed magnetic maps as well as the most thorough lunar gravitational atlas to date, which reveals hidden concentrations of mass. "These [gravity field] images are remarkable in their clarity," says geophysicist Gregory Neumann of the Massachusetts Institute of Technology and NASA's Goddard Space Flight Center in Greenbelt, Maryland. "They resolve aspects of the moon that we couldn't see before."

Researchers charted the moon's gravitational peaks and valleys by using Earth-based radio telescopes to track gravity's subtle tugs on Prospector. The resulting map let them calculate how mass is parceled out in the moon's interior five times more precisely than before, says team leader Alex Konopliv of NASA's Jet Propulsion Laboratory in Pasadena, California. The calculations indirectly constrain the core's radius to between 220 and 450 kilometers—toward the small end of the range if the core is pure iron, and toward the larger end if it is made of a less dense alloy such as iron sulfide.

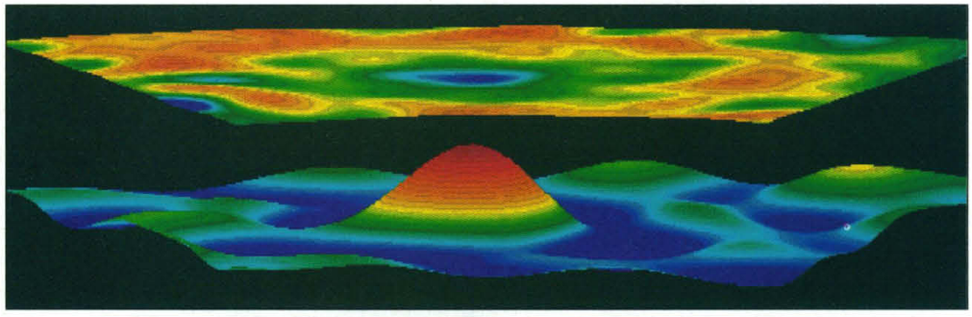
Such a core would hold 1% to 4% of the moon's mass, says the team. That's good news for proponents of the leading theory of the moon's birth: that it coalesced from the debris of an impact between a Mars-sized protoplanet and the half-formed Earth, 50 million years after the solar system arose. "The giant-impact theory has no problem explaining a core of that size," says planetary scientist Robin Canup of the Southwest Research Institute in Boulder, Colorado. The iron came mostly from the shattered core of the impactor, according to models by Canup and astrophysicist Alastair Cameron of the Harvard-Smithsonian Center for Astrophysics in Cambridge, Massachusetts. Other scenarios of lunar origin, such as coformation with Earth, capture of a large asteroid, or fission from the young Earth's mantle, call for a larger iron core or none at all, Canup notes.

Lunar Prospector's gravity survey also exposed several new "mascons," dense blobs of rock, beneath impact basins that are not filled with smooth lava. This suggests that the stronger pull of gravity over these areas results from plugs of dense material that rose toward the surface from the mantle, rather than from lava fills, Konopliv says. "That's a surprising result," says planetary geophysicist Roger Phillips of Washington University in St. Louis. "It means the moon's outer layers must have cooled off rapidly, within half a billion years, to become rigid enough to support mantle upwarpings."

Refining the moon's early thermal history may help scientists understand how long the core itself stayed hot. Prospector data suggest it remained molten until at least 3.6 billion years ago, when the era of giant impacts on the surface came to an end. The probe's magnetometer picked up traces of magnetism locked into patches of crust—perhaps sites where big impacts shocked the rocks strongly enough for them to capture an imprint of the magnetic field. The strength of this fossil field implies that at the time, the dynamo action of flowing metal in the core was generating a magnetic field perhaps as strong as Earth's today.

One patch of lunar crust is so intensely magnetized, in fact, that it deflects the solar wind's charged particles away from the surface, just as Earth's own magnetic field does. The phenomenon, first seen in less detail by the Explorer 35 orbiter in 1967, could be "a signature of a strong dynamo field from a molten iron core in the past," says physicist Robert Lin of the University of California, Berkeley. However, magnetic-field expert Norman Ness of the University of Delaware, Newark, cautions that the crustal imprints could have come from a strong interplanetary magnetic field rather than one internal to the moon.

The gravity and magnetic data seem to "tell a consistent story" about the moon's core, says planetary scientist Lon Hood of the University of Arizona, Tucson, a co-author on both studies. Future probes such as next year's Japanese Lunar-A mission, which will take seismic x-rays of the moon by im-



ALEX KONOPLIV, NASA JPL/CALTECH

Lunar lump. A new gravity survey by Lunar Prospector suggests that a plug of dense mantle material (red, bottom) underlies the Mendel-Rydberg impact basin (blue, top).