Disease Puzzle Nears Solution

In November of last year the first reports of a strange new epidemic came from New Mexico. The varied symptoms included severe muscle pain and abnormally high numbers of eosinophils, a type of white blood cell. The disease, dubbed eosinophilia-myalgia syndrome (EMS) was clearly not infectious, and it was soon realized that all the victims had been taking the amino acid L-tryptophan, which is widely sold over the counter as a "natural" tranquilizer and sleeping pill.

Since then more than 1500 cases of EMS have been reported to the Centers for Disease Control, along with 24 deaths. But speaking at the first international conference on EMS, which took place last month at the Los Alamos National Laboratory, Henry Falk of the CDC reported that the actual number of cases may be much higher: as many as 5,000 to 10,000. It was also reported that a specific impurity—probably stemming from a bacterial strain—in lots of L-tryptophan made by a single Japanese manufacturer may be the cause of the syndrome.

The impurity, known as "peak E," was identified by high-performance liquid chromatography, according to Edward Belongia of the Minnesota Department of Health. The CDC had earlier reported that the L-tryptophan taken by almost all EMS victims was produced by Showa Denko, a huge Japanese chemical and pharmaceutical company. Belongia reported to the conference that peak E was found in the samples of Showa Denko's L-tryptophan tied to EMS cases but not in any other samples.

He added that all the L-tryptophan related to EMS cases came from a small number of Showa Denko lots produced between October 1988 and June 1989. That period coincided with the introduction of a new strain of the bacillus that is used as a "factory" in the production of the amino acid; it appears that the impurity is also a fermentation product.

Is peak E, in fact, the cause of the puzzling new syndrome? Many researchers believe that to be the case, although it may turn out to be only a marker for the true pathogenic agent. Strenuous efforts are now being made to find the chemical structure of peak E, according to Samuel Page, head of the natural products and instrumentation branch of the U.S. Food and Drug Administration.

But those efforts have been hampered by the extremely small samples available: the amount of the impurity in each tablet was exceedingly small. "We have only a few micrograms of this substance to work with," Page said. "If we had 10 milligrams we could have the answer in a few hours." Despite the difficulties, Page said he hoped the impurity would be identified soon.

The EMS episode raises serious questions for the emerging biotechnology industry. CDC's Falk told the conference that all the case-related samples were well within the 98.5% purity limits set by the FDA. But, Falk added, "98.5% purity doesn't mean very much when we're talking about biologically active contaminants that, in varying minuscule quantities, can create powerful effects. He added that the issue of biologically active contaminants will have implications for biotech because many of its products are synthesized by bacteria.

EMS is now known to be a complex systemic syndrome with inflammatory and autoimmune components that affect the skin, fascia, muscle, nerve, blood vessels, lung, and heart. Andrew Engel, a pathologist at the Mayo Clinic, used the image of "dynamite in a lake" to describe EMS: enormous disruption has taken place, but to sort out the precise sequence of events is quite difficult. Although it was initially thought that the destructive effects of eosinophils were responsible for most of the pathology, it is now clear that many other systems are involved, including macrophages, and fibroblasts, along with lymphokines and other chemical messengers.

The syndrome may help clear up other medical mysteries, Esther M. Sternberg of the National Institute of Health and the National Institute of Mental Health told *Science*. Little is now known about what initiates inflammatory and autoimmune diseases, she said. "Once we have identified the initial inflammatory trigger in EMS," she added, "we will be able to elucidate the way it interacts with the complex cascade of secondary events." ■ **PHILIP RAPHALS**

Philip Raphals is a free-lance writer based in Montreal.

Scientists Protest Museum Cuts

Last April the Board of Trustees of the venerable British Museum of Natural History approved a plan intended to bring the museum into the future—by surgical cutbacks of some of its traditional strengths. Proposed by director Neil Chalmers, the plan would eliminate 50 research posts, drastically reducing research on fossil plants and mammals. That plan has aroused great concern among researchers, who fear that the museum's scientific treasure—collections that include 67 million plant and animal specimens—will lose its vitality in the absence of ongoing research. And some fear the cuts may ultimately threaten the existence of the collections themselves.

These possibilities have driven the research staff of the museum to fight back. Their secret weapon: the international scientific community. When the plan was announced, museum staffers began sending information packets to colleagues around the world, asking them to write in protest to Chalmers, the Board of Trustees, members of Parliament—even Maggie Thatcher herself.

The scientific community's response was fiercely supportive, including large numbers from the United States. Former Minister of Arts Richard Luce, whose ministry is responsible for the museum, got more than 900 letters before he resigned on 23 July (for reasons unrelated to the museum fuss). And the debate has spilled over the banks of normally staid academic discourse. One June evening the House of Commons stayed up until 3:30 in the morning talking heatedly about the Jurassic flora of Yorkshire and the shield bugs of Surinam.

Behind such Pickwickian scenes lurk scientific issues. Under the Chalmers plan, museum research is to concentrate on six areas "relevant to contemporary needs and issues," such as human origins, human health, and the environment. Curatorial and research functions are to be separated. And without ongoing research to determine what specimens should be added and how existing groups should be reorganized, many scientists think the collections will wither. "Dead collections are those that aren't growing or used—they're just stored. That's what's happening to the British Museum—it's going from being a live museum to being a dead one," Vicki Funk, a plant systematist at the Smithsonian—and a protest-letter writer—told *Science*.

Another American letter writer, Richard Kay, chairman of the department of biological anthropology and anatomy at Duke, agreed that the collections are critical and that they must be coupled with current research. "I think a portion of the scientific community may see these collections as a refreshing breath of the 19th century. What they fail to see is that we're losing habitat and increasingly endangering species worldwide, and we can't even begin to assess this

problem without systematics collections."

The American response included not only individuals but also institutions. In a letter of 14 June, the Senate of Scientists of the Smithsonian charged that the Chalmers plan ignores the museum's traditional strengths and will "further contribute to the dissembly of a world-renowned group of scientists."

But Chalmers thinks the critics are way off base. In particular, he thinks that a trans-Atlantic cultural gap may get in the way of Americans understanding what he's up to. "People in the States may not understand what we mean by research and what we mean by curation," he asserts. In particular, he points out that biodiversity will be a major focus. No single institution can research all forms of life, he argues, and adds that curation will improve, despite the loss of some research.

But those assurances haven't fully calmed the waters. And some scientists are concerned not just about the British Museum, but also about the effect that cuts there may have, directly or indirectly, on research elsewhere. As the Smithsonian's Funk says: "It could have a definite impact elsewhere. We're all running a little scared around here." ■ ELIZABETH CULOTTA

Elizabeth Culotta is a science writer at the Milwaukee Journal.

Mouse Facility Makes a Comeback

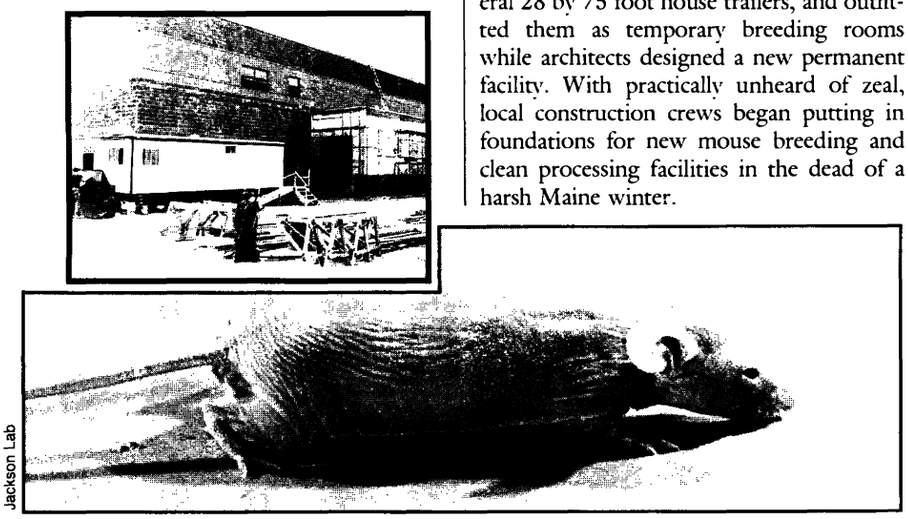
Bar Harbor, Maine

Thanks to a combination of resourcefulness and financial derring-do, the mouse breeding operation at the Jackson Laboratory in Bar Harbor, Maine, has risen from the ashes. Just 15 months after a fire wiped out all of the lab's production offices and sterilization facilities, and most of the mouse rooms and breeding stock, the lab has returned to nearly 80% of its prefire production capacity. But precarious financial times lie ahead, and there are lingering questions about the propriety of a $10-million federal handout that the nonprofit lab is counting on to proceed with its recovery.

The Jackson Laboratory is an unusual hybrid. On the one hand, it is a research institute, carrying out basic genetic studies on mice. On the other, it has become a unique repository and supplier of rare inbred and mutant strains of mice to researchers around the world. Before the 10 May 1989 fire, the lab was producing approximately 2 million mice per year. It has foundation stocks for some 1700 genetically different strains, and in 1988 it distributed 490 strains to other laboratories. According to a survey commissioned by the lab, when fire interrupted the supply of JAX mice, research valued at $600 to $700 million per year was affected. Many research projects simply ground to a halt.

Kenneth Paigen, who left the University of California at Berkeley to become the Jackson lab director shortly after the fire, says the lab's first decision was whether to rebuild at all, or simply use the insurance settlement as an endowment for the research institute. Convinced that the lab provided a crucial research resource, Paigen says the lab decided to rebuild—and do it as quickly as possible. "We assumed we could build faster than the mice could breed," he says.

The first step was to commandeer every space remaining anywhere on the campus for mouse production. The lab bought several 28 by 75 foot house trailers, and outfitted them as temporary breeding rooms while architects designed a new permanent facility. With practically unheard of zeal, local construction crews began putting in foundations for new mouse breeding and clean processing facilities in the dead of a harsh Maine winter.



Jackson Lab

Mouse house. *Jackson Lab's nude mice have a new $30-million home (inset).*

But putting things on the fast track meant spending money—lots of it. The lab estimates that the $10.8-million insurance settlement will cover only about a third of the final recovery costs. So they looked for a benefactor, and found one in Congress. Congress authorized $15 million in new construction authority for the National Institutes of Health, $10 million of which was made available to anyone who wanted to build a new mouse breeding facility. The legislative language was chosen carefully to avoid charges of pork barrel politics, but lab officials say as far as they know, the Jackson Lab is the only one competing for the money. Even if they get the $10 million, as seems likely, the lab still must find an additional $10 million to finish the reconstruction program. Paigen says he is hopeful that Congress will ante up a second time, but the recently approved House appropriation for NIH does not contain the construction money. Paigen thinks the Senate will add it in its version of the appropriations bill, and that it will survive in the final version approved by both houses.

Not everyone is pleased with the decision to make federal money available to Jackson Lab. Commercial mouse breeders like Charles River Laboratories and Harlan Sprague-Dawley have maintained that the lab is a commercial competitor and is getting an unfair boost. They say Jackson Lab officials spurned their offers of help following the fire and have consistently refused offers to sublicense some of the more popular JAX mice strains to prevent supply interruptions in the event of future catastrophes.

Lab officials counter that they need to keep selling the popular strains to subsidize the rare mutant lines that could never generate adequate revenue to keep the lab going. They also point out that by keeping a large volume of breeding mice, they have been able to identify and isolate approximately 20 new naturally arising mutant strains each year. For example, a mutant mouse with lysosomal storage disease now being studied by Edward H. Birkenmeier at the lab arose in a normal C57BL/6 mouse. A commercial facility might simply have discarded the unhealthy animal.

NIH officials made a site visit to Bar Harbor last week to review the lab's application for a federal grant. A decision is expected before the end of the fiscal year, 30 September. Paigen says taking a conservative financial course would have delayed returning to full capacity by 2½ years. Instead, he says they decided to start building and gamble they would recover the funds later. With so much research waiting on JAX mice, "We didn't feel we had an option," he says. ■ JOSEPH PALCA