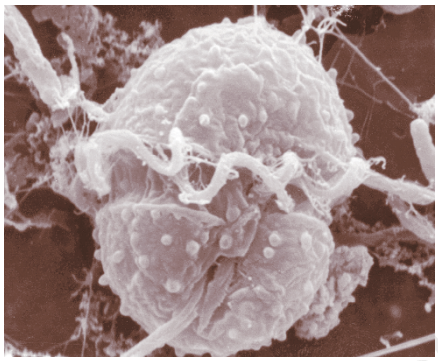
Scientists close in on 'cell from hell' lurking in Chesapeake Bay

KAREN STEIDINGER



KAREN TAM/AP

Toxic shocker: the organisms blamed for fish kills are related to *Pfiesteria piscicida* (left), whose discoverer, JoAnn Burkholder (right), blames it for neurological symptoms she has experienced.

[WASHINGTON] A mystery organism which is believed to have killed thousands of fish in Chesapeake Bay, on America's mid-Atlantic coast, and prompted a major public health scare, should become less mysterious within weeks as scientists rush to track down the organism and identify the toxins it releases.

Multi-agency research is already under way to investigate the dinoflagellates, which are thought to have killed some fish and caused large lesions on many others. According to an early study, fishermen who work the infected waters have suffered memory loss and skin problems. The infected fish are menhaden, which is never eaten but is harvested in huge quantities for use in pet-food and as a source of cheap oil for margarine.

But the scientists who pioneered the study of similar organisms claim their investigations have been obstructed by officials in the nearby state of North Carolina, who wanted to protect their tourism, fisheries and agriculture industries from the kind of public attention now developing in Maryland.

The organisms in the Chesapeake — a 200-mile-long sea inlet whose health and conservation is a major public concern in the region around Washington — are closely related to *Pfiesteria piscicida*, a remarkable single-cell organism first identified five years ago by JoAnn Burkholder of North Carolina State University (see *Nature* **358**, 407; 1992).

Pfiesteria can take twenty or more distinct forms during its life cycle. It can play dead on the sea bed, grow via photosynthesis, secrete toxins, eat the fish poisoned by the toxins, and return to an ambient state — to be branded "the cell from hell" by *The New York Times*.

"Of all the organisms I know, it's the most complex by a quantum jump," says Donald Anderson of the Woods Hole Oceanic Institute, Massachusetts. "It's hard to understand how it evolved that way. But if you wanted an organism that would survive for millions of years, that would be a good way to do it."

Burkholder found that *Pfiesteria* growth was boosted by the presence of phosphorus in the water, and became embroiled in arguments with North Carolina officials about the role of the effluent from the state's hog-farming industry in the organism's behaviour. Burkholder and Howard Glasgow, her collaborator, suffered neurological symptoms which they attributed to their contact with *Pfiesteria* in the laboratory. Their story is related in a recently published melodrama*.

Ironically, the suspicion that *Pfiesteria* is a health hazard has slowed down research on the organism. Scientists could not study it unless their laboratories met standards for the containment of biological hazards, which are rare in marine biology laboratories.

But since fish kills were reported in Chesapeake Bay just over a month ago, Burkholder and a few others have won access to medical laboratories for the analysis, and have made substantial progress in identifying the toxins released by *Pfiesteria*. They have also been adopted as advisers to the state governments confronting the problem.

Burkholder is working with the Medical University of South Carolina to track down a toxin associated with brain damage in fish. Edward Noga, her *Nature* co-author, has worked with researchers at the University of Miami on a separate toxin that may cause lesions on the fish. "We've made great strides in the past three weeks, thanks to the help of these places," Burkholder says. "We've isolated a water-soluble toxin and a lipid-soluble toxin, and are very close to finding out what the water-soluble toxin is."

But Karen Steidinger of the Florida Marine Research Institute, who has been analysing water samples from Chesapeake Bay, says that the two dinoflagellates she has identified are not *Pfiesteria*. "Once you take off their membrane, they are very different," she says. Although closely related to *Pfiesteria*, these organisms could produce different toxins that interact differently with fish and with people, she says.

A study conducted in the past three weeks for the Maryland state government, by a team led by Glenn Morris of the University of Maryland School of Medicine, found a strong correlation between exposure to water near the fish kill and various neurocognitive symptoms. The study compared a self-selected sample of eleven fishermen who worked the Pocomoke river, where a major fish kill occurred in August, with a group which may have received lower exposure, and a third group which works nearby on the Atlantic Ocean and is assumed to have had no exposure at all. "We found a significant problem with memory loss" in the high-exposure group, Morris says. "There do appear to be clear, documentable health effects."

Steidinger, however, says that the correlation itself does not prove that people have been poisoned by the *Pfiesteria*-like organisms. The dead fish themselves, she points out, will put toxins in the water: cause and

**And the Waters Turned to Blood*, by Rodney Barker, $24 from Simon & Schuster.

EPA to be sued over gene-modified crops

[WASHINGTON] The US Environmental Protection Agency (EPA) learned last week that a coalition of consumers, environmentalists and organic farmers intends to sue it for allowing the planting of crops genetically engineered to produce an insecticidal toxin made by *Bacillus thuringiensis* (*Bt*) a soil bacterium.

Thirty signatories filed a petition with the EPA demanding that it revoke 11 registrations it has issued to five companies to plant modified corn, cotton and potatoes. The petition also asks the agency to cease granting such permissions, and to complete a statement analysing the environmental impact of *Bt* crops approved so far.

The petitioners claim that commercial planting of the crops threatens to create widespread resistance to *Bt* toxin, which is heavily relied on by organic farmers.

Al Heier, an EPA spokesman, said the agency "will consider the petition very seriously". But he argued that the EPA won approval from a panel of outside scientists before agreeing to register the first *Bt* crop in 1995.

Meredith Wadman

effect can be established only by identifying and tracking the toxins from the organisms.

The Morris study, which was released last week, has been the subject of some disagreement between Maryland and Virginia, the two states surrounding the bay, with the former unwilling at first to hand over its raw data for scrutiny by the latter.

The Democrat governor of Maryland, Parris Glendening, who is up for re-election next year, has sought to impress the largely urban voters of his state by taking immediate, high-profile action on the fish kills. He has closed several rivers to fishing, and obtained federal assistance and pledges of public concern from President Bill Clinton.

Virginia is taking a far more cautious approach. George Allan, its Republican governor, has refused to close any rivers apart from the Pocomoke itself, despite the discovery of fish with lesions in other waterways.

The two men buried some of their differences at a 'governors' summit' hosted by Glendening last week in Annapolis, Maryland's capital, at which they agreed a five-point plan to cooperate in addressing the problem. Allan continues to express doubts about the Morris study, however. "The number of people who reported memory loss was, I believe, eight," he says. "Our medical professionals haven't had the chance to look at it yet. I'd want our folks to look over it and see if they come to the same conclusions."

A barrage of small-scale federal initiatives was announced last week to pursue the mystery organism. The Environmental Protection Agency (EPA) and the National Oceanic and Atmospheric Administration have sent teams to the bay and will provide Maryland with emergency grants.

The Centers for Disease Control, which is expected to receive an emergency $7-million appropriation from Congress for *Pfiesteria* research, will host a conference in Atlanta next week to "plan a comprehensive public health approach to *Pfiesteria*".

The Food and Drug Administration is expected to explore any possibility that toxins from the organism could enter the food chain through menhaden. There is no evidence so far that the toxins accumulate in the fish, officials say.

Pressure for action to restrict the run-off of nutrients from Maryland's large chicken industry in response to the incidents appears to be waning, however. A plan is already in place to cut these by 40 per cent, and Glendening says he has no plans to legislate further.

Carol Browner, EPA's administrator, who attended the Annapolis meeting, said that the fish kills were "a clarion call" to address the flow of nutrients and other pollution into natural waterways. Not everyone is convinced, however. As Karen Steidinger points out, Spanish explorers of the Florida coast were warned about annual fish kills by the Indians — in 1560. **Colin Macilwain**

Cancer scientist takes on top job at Wellcome Trust

[LONDON] Britain's Wellcome Trust, which describes itself as "the world's biggest medical research charity", has chosen a prominent cancer researcher to lead it into the next century.

Mike Dexter, only recently appointed director of the Paterson Institute in Manchester, which is largely funded by the Cancer Research Campaign, will succeed Dame Bridget Ogilvie on her retirement next year.

There had been discussion about whether the trust, whose capital assets, estimated to be worth more than £10 billion ($16 billion), are even larger than those of the Howard Hughes Medical Institute in the United States, might turn to the business community to recruit its new chief executive.

Instead, the trustees have chosen a widely respected haematologist with experience both as a researcher — he has published more than 300 scientific papers — and in research administration as, for example, chairman of the Medical Research Council (MRC)'s molecular and cellular medicine board.

As one of the three co-founders of Therxsys, Britain's first gene-therapy start-up company which is partly owned by the MRC and has rights to key MRC research on gene vectors, Dexter also has direct experience of working on the commercial applications of scientific discoveries, an increasingly important dimension of the trust's activity.

Dexter says the trust, which has recently taken a lead in establishing a clear career structure for research scientists, "has a responsibility to stand up for the scientific community, and to make sure that funding goes to where the science is excellent, not necesssarily where some other organization would like it to go".

WELLCOME TRUST

Dexter: believes the trust 'has a responsibility to stand up for the scientific community'.

Having been closely involved in gene-therapy research in Manchester, Dexter says he is keen to support the trust's growing involvement in issues concerned with the public understanding of science — and particularly exploring the implications of modern genetics. "It is important that we bring the public along with us," he says.

Dexter's appointment is described as "inspirational" by Gordon McVie, director-general of the Cancer Research Campaign, which has supported Dexter's research since the early 1970s.

"He has a wealth of experience in biology and a terrific grasp of the technical side of experiments, and the fact that he comes from the cancer side of things is no drawback, as we have been closely linked with many important developments in genetics in recent years," says McVie. Ironically, Sir Henry Wellcome specified in his will setting up the trust in 1936 that no money was to be used for cancer research as such. **David Dickson**

£10 million pledged for UK synchrotron source

[LONDON] In an unprecedented move, the Wellcome Trust has announced it is prepared to contribute £10 million to the costs of a new second-generation synchrotron source, known as Diamond, at the Daresbury laboratories in Cheshire, England.

The offer comes as various research councils have been asked by the Office of Science and Technology to give their views on a replacement for Daresbury's current 2-GeV Synchrotron Radiation Source (SRS) which becomes obsolete early in the next decade.

The heavy use of the facility by researchers has left little doubt that the research councils will be positive. But that will leave open the question of who is prepared to pay for what.

Current estimates are that a new storage ring will cost £100 million – a sum the research councils hope will be found by central government – and that experimental beam lines would cost another £40 million, which the research councils might find out of their own budgets.

Officials of Wellcome Trust have in the past said that the trust should not be expected to make up for the government's failures to maintain a healthy research infra-structure, so the trust may be reluctant to contribute towards the costs of the ring itself.

Despite this uncertainty, David Norman, director of the SRS facility, says he hopes the Wellcome offer will "catalyse" thinking about the value of the facility both in the research councils and in government circles. **D.D.**