Diagnosis of *Pfiesteria*-human illness syndrome

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ABSTRACT: The first case reports of human illness caused by exposure to *Pfiesteria piscicida* toxin(s) acquired outside of a laboratory are reported. Though *Pfiesteria*, a toxinforming dinoflagellate, is responsible for killing billions of fish in estuaries in North Carolina, its role in human illness has remained controversial, in part due to lack of identification of the toxin. A recent fish kill in the rivers of the lower Eastern Shore has permitted careful investigation and identification of a distinct clinical syndrome resulting from exposure to the *Pfiesteria* toxin — *Pfiesteria human illness syndrome* (PHIS). Patients have memory losses, cognitive impairments, headaches, skin rashes, abdominal pain, secretory diarrhea, conjunctival irritation, and bronchospasm. Not all patients have all elements of the syndrome.

A cluster of patients have exhibited signs and symptoms after contact with water, aerosol, or water droplets containing toxins from *Pfiesteria piscicida*. *Pfiesteria* is a dinoflagellate with small, toxic forms called zoospores and large nontoxic amoeba forms. Despite the documented presence of *Pfiesteria* in Maryland’s Chesapeake Bay, and the Neuse River and Pamlico Sound in North Carolina, there were no prior reports of an association of *Pfiesteria* in the wild and subsequent human illness.

This report is the first to associate *Pfiesteria* toxin exposure with acute human illness. Discharge summaries of five patients I saw fit this presumption. As more is learned, additional information will be pre-
sented, hopefully with details as to etiology, prevention, and therapy.

Case 1

The patient is a 23-year-old white man who had watersked 500 yards downstream from the site of a fish kill (Shelltown) that occurred the following week. He had been in the water for approximately one hour, having fallen rather frequently. He had been healthy before exposure. Within three hours he began experiencing a severe pounding headache with reduced recent memory, as well as abrupt onset of nausea and dizziness. Because of these symptoms, he retired early. The following morning he awoke with an increasing headache and approximately 30 unusual skin lesions arrayed in an asymmetric distribution on his lower extremities and groin. The lesions, measuring 1.5 cm to 2 cm in diameter, had circumscribed borders that were slightly pruritic, displaying evidence of follicular eruption without evidence of cellulitis. Routine cultures were negative. No fungi, hyphae, or spores were noted. The lesions were similar to those seen by physicians in a laboratory in New Bern, North Carolina.

Skin biopsy showed a significant eosinophilic infiltration with a nonspecific inflammatory response. No induration, central punctum, raised edges, or skin atrophy were noted. Skin lines were maintained and a few petechiae were seen. The patient was treated with a potent steroid topically; no other medications were administered. The tentative diagnosis of human pfiesteriosis was made.

The patient continued to have severe headaches three days later, at which time the patient also complained of mild shortness of breath. The patient’s brother, who had less water exposure on the same day, also noted similar skin lesions. Over the next several days the patient deteriorated, developing a severe stiff neck and changes in his mental status including difficulty in recent memory, mild dysarthria, mild ataxia, and mild difficulty in rapid alternating movements.

The patient was admitted to the local hospital. Computerized axial tomography scan of the brain was normal. Magnetic resonance imaging revealed some mild inflammation of the mastoid and a possible polyp in the sinuses. The spinal fluid was clear with a total protein value of 27 and a glucose value of 59, and a simultaneous blood sugar value of 90 (all normal values). Two cells were found. A comprehensive battery of studies done on the spinal fluid did not show any additional abnormalities. He was treated with nonsteroidal antiinflammatory drugs for his headache; however, his mental status did not resolve. Because of this persistent abnormality, the patient was referred to Dr. Donald Schmechel at Duke University, who has evaluated patients with possible Pfiesteria-related illnesses in the past. Dr. Schmechel’s evaluation showed persistent defect in memory with specific abnormalities in psychometric testing. He thought the neurocognitive defect was, to a reasonable degree of medical certainty, related to the Pfiesteria exposure.

Case 2

The patient is a 26-year-old white man who was swimming in the Pocomoke River on the same day as the waterskier in Case 1. He was somewhat upstream from the Shelltown area. He had an abrupt onset of two lesions, one on his forehead and one on the nose, each approximately 1.5 cm x 2.5 cm. There was a difference in the forehead lesion in this case when compared with the index case. At first glance, this lesion looked like a tinea-type infection but there was no scale, KOH preparation was negative, and the edges were not indurated. The lesion on the nose was more typical of those seen on fish affected by Pfiesteria. Biopsy of this lesion showed an eosinophilic infiltrate on a non-specific inflammatory background. He was treated with topical steroids and made an excellent recovery. There were no additional symptoms or neurologic, respiratory, or gastrointestinal problems. The patient was seen for follow-up on August 13, 1997, with full recovery.

Case 3

This patient is a 30-year-old white woman who was swimming with her children in the Pocomoke River in the vicinity of the waterskier (Case 1). She related that she experienced an abrupt onset of nausea, a profuse watery diarrhea, and headaches after the river exposure. She had a mild loss of appetite. At first, the diarrhea was osmotic (i.e., it was worse after she ate something), but later it became secretory with nocturnal bowel movements. The diarrhea was watery with associated urgency and without blood or mucus. Stool cultures were attempted, but specimens were not satisfactory. Examinations for ova and parasites were negative.

The patient had a sharp periumbilical crampy abdominal pain in association with her headaches, which she described as daily and bitemporal. The pain was not associ-
ated with temporomandibular joint pain nor with any trapezius muscle spasm. She had previously been well with neither abnormal social stresses nor abnormal bowel history. She reported that she had been using full bottles of Kapectate and Pepto Bismol without relief. The patient was treated with Cipro, which is used to treat travelers’ diarrhea. After four days her symptoms did not improve. She was given cholestyramine as a bile salt binder. The patient improved quickly over three days. She was well two weeks later. Her headaches cleared as the diarrhea abated.

Case 4

The patient is a Department of the Environment worker who was sorting fish at Shelltown during the active fish kill the first week of August. She was wearing protective gloves extending to her wrists. Her shirt left her forearms exposed, resulting in significant river water splash on this area. Her forearm felt burned; the sensation persisted despite washing with distilled water. Within six hours she began noticing memory problems as well as a productive cough and wheezing. The memory problems were such that she reported she went to the grocery store three times with a list and on each occasion returned home without completing her list because she could not figure out what she was supposed to purchase.

The next day, a rash appeared on her exposed forearm with small blisters that became confluent. Two days later, desquamation of the skin of the right forearm was noted. Her skin healed in about one week. A biopsy was obtained but was nondiagnostic. Because her mental status abnormalities persisted, she was referred to Dr. Schmechel at Duke University for confirmation of possible Pfiesteria-related toxic exposure and toxic dermatitis. Her psychometric tests at Duke were similar to those of the laboratory worker exposed to the Pfiesteria toxin and the waterskier (Case 1). Dr. Schmechel concurred with the diagnosis.

Case 5

The patient is a 41-year-old state worker whose job of 20 years included sampling shellfish beds for fecal coliforms. He had no history of health problems related to the river. The sampling required that he use a device attached to a rod that was immersed to obtain water samples. He held the rod in his right hand and pulled the wet sample tube off the rod with his ungloved left hand. Soon after exposure on August 5, 1997, he noted development of three lesions but only on the fingers of his left hand. These went on to desquamate as in the patient described in Case 4. The desquamation was pronounced at the distal tufts and at the posterior nail folds. He had what he called a “hot spot” in his mid-palm that had persisted for the previous two weeks. This lesion was similar to the index case; it was a discrete macule with maintenance of skin lines but with no evidence of scale or any evidence to suggest an insect bite. He felt that the burning in his hand stemmed from the mid-palm macular lesion. When this area was biopsied, he stated that the lidocaine completely stopped the burning for the first time in two weeks.

The patient stated that his memory was reduced from his previous status, pointing out that he had forgotten to call a co-worker, something he normally would not forget to do. He also described a watery diarrhea without blood or mucus which was associated with a crampy periumbilical pain. His skin biopsy was also not diagnostic. He recovered without treatment.

These cases were among others later evaluated by the Department of Health and Mental Hygiene expert physician panel. To date I have referred 33 patients for psychometric testing. The psychometrics give a consistent “fingerprint” of abnormalities seen with Pfiesteria exposure but not with controls. The clinical syndrome is variable but memory loss, secretory diarrhea, conjunctivitis, skin rash, headache, and bronchospasm all may occur.

Continued use of cholestyramine has not only ameliorated diarrhea, but also has helped improve memory loss and asthma-like symptoms.

The lack of illness following eating seafood harvested from the affected waters suggests instability of the toxins in food or destruction of toxins by digestive mechanisms.