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IMPLICATIONS OF HARMFUL MICROALGAE AND HETEROTROPHIC DINOFLAGELLATES IN MANAGEMENT OF SUSTAINABLE MARINE FISHERIES

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Abstract. Worldwide increases in the frequency and spatial extent of blooms of harmful marine microalgae and heterotrophic dinoflagellates suggest that these species are becoming an increasingly important influence on year class strength of marine fishes through both direct and indirect mechanisms. Impacts on fish populations from harmful marine microalgae and heterotrophic dinoflagellates have been considered primarily from the limited view of acute or lethal influences. Accumulating evidence indicates that insidious sublethal and chronic impacts to both fish and human health from these organisms, such as long-term behavior alteration, increased susceptibility to cancers and other diseases, depressed feeding, and impaired reproduction, may be substantial and pervasive. For some harmful species, significant indirect impacts that promote critical habitat loss or disrupt the microbial food web balance also have been documented. Because successful models to predict the behavior and growth of most of these species have not yet been developed, and because toxins for many are poorly characterized, a clear anthropocentric focus has guided management strategies for confronting their outbreaks. The extent to which management takes the fundamental step of acknowledging scientifically demonstrated linkages among harmful microalgae, shellfish contamination, fish kills, and human health impacts has also been seriously constrained by political dictates stemming from economic considerations. Without federal involvement, and without catastrophe of human death or widescale serious human illness, little progress historically has been realized in the development of effective management strategies to mitigate lethal impacts to fish or other organisms. Many long-known taxa such as certain "red tide" dinoflagellates apparently can increase independently of human influences other than physical transport. However, some newly discovered toxic or otherwise harmful taxa have been correlated with cultural eutrophication in poorly flushed fish nursery grounds such as estuaries and coastal waters. Outbreaks of certain warm-optimal species have coincided with El Niño events, suggesting that warming trends in global climate change may stimulate their growth and extend or shift their range. The available information points to a critical need for a more proactive, concerted effort to determine the full range of chronic/sublethal effects, as well as acute impacts, on marine fish populations by harmful marine microalgae and heterotrophic dinoflagellates, so that their increasingly important influence can be factored into reliable plans for sustainable fisheries management.

Key words: algae, toxic; coastal waters; estuaries; eutrophication; fish health; fish kills; harmful algal blooms; heterotrophic dinoflagellates; shellfish.

Introduction

As states and nations battle over the ocean's fishing grounds with harvest efforts increasing and many wild stocks in decline (Holmes 1994, Pauly and Christensen 1995), more subtle but significant influences on fish populations have been largely ignored in policy considerations (Tibbetts 1994, Beddington 1995). Some of these factors, such as habitat quality and changing food web structure, are under both stochastic and anthropogenic influences. Among the more enigmatic food web components that appear to be increasing in frequency and extent are blooms of harmful marine microalgae and heterotrophic dinoflagellates (Smayda 1989, Lom and Dykova 1992, Hallegraeff 1993, Burkholder et al. 1995*a*). These organisms include species that have directly or indirectly caused the death of billions of finfish and shellfish in events dating back thousands of years (Steidinger and Baden 1984, Dale et al. 1993), as well as more recently discovered taxa with apparent stimulation by human activities (Hallegraeff 1993).

Despite the apparent increase in outbreaks by harmful marine microalgae, there has been little progress in

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predicting or controlling their toxic outbreaks, or even in mitigating their economic or ecological impacts (Taylor 1987, Anderson 1995). Although the activities of harmful microalgae are sometimes correlated with coastal development (Lam and Ho 1989, Hallegraeff 1993), their responses to nutrient enrichment remain poorly characterized. Outbreaks sometimes occur in areas with sparse cyst "banks" or dormant cells that could re-establish active growth during subsequent growing seasons, while embayments with more abundant cysts produce few active cells (Steidinger and Baden 1984, Taylor 1987). Some or, more likely, many of the species have complex life cycles with multiple stages and morphs that respond to a diverse array of physical, chemical, and trophic conditions (Estep and MacIntyre 1989, Burkholder and Glasgow 1995, Landsberg et al. 1995). Accumulating evidence of serious impacts to marine fish populations by harmful marine microalgae points to a critical need for their more rigorous evaluation in fisheries management issues. Here, current understanding about the role of these organisms in management of sustainable fisheries is examined, from consideration of both acute and chronic impacts on the survival and viability of fish populations. Examples of current regulatory responses to outbreaks of harmful marine microalgae and heterotrophic dinoflagellates are presented, and considerations are suggested for future research and policy directions in confronting the uncertainty they impart to marine fisheries management.

Recent History of Outbreaks

There is growing consensus among scientists that the past decade has yielded a global increase in marine microalgae that are harmful to finfish, shellfish, and their human consumers (Smayda 1990, Hallegraeff 1993, Anderson 1995, Shumway 1995). Toxic dinoflagellates (Pyrrhophyta, Desmophyceae, and Dinophyceae), for example, numbered 22 known species in 1984 (Steidinger and Baden 1984), but increased to 59 species a little more than a decade later (Table 1). Geographic expansion of known toxic species has been linked, in some cases, to introductions by ballast water transport along shipping routes (Hallegraeff et al. 1990, Carlton and Geller 1993). Whereas most of the long-known harmful taxa appeared to operate independently from human influences other than physical transport (Steidinger and Baden 1984, Tester et al. 1991), various newly discovered taxa first were reported from quiet, poorly flushed estuaries and coastal embayments under cultural eutrophication (Smayda 1989, Hallegraeff 1993; Table 2)—a descriptor that increasingly characterizes many coastlands throughout the world (Monbet 1992, DeFur and Rader 1995). The recently known toxic representatives include species that formerly were described as benign (Wright et al. 1989), as well as species from the "hidden flora" (Smayda 1989) that previously had not been detected (e.g., Kaas et al. 1991, Burkholder et al. 1992). Data on water column nutrient supply ratios have shown shifts over the long term that were linked to increased anthropogenic loadings (Smayda 1989). These correlative field data, coupled with experimental evidence, suggest that some algal species that are not normally toxic may become so when exposed to altered nutrient regimes from excessive overenrichment (Shilo 1987, Smayda 1989, Evardsen et al. 1990, Bates et al. 1991, Hallegraeff 1993). Outbreaks of some species also have coincided with El Niño events, and this observation, considered with the tendency for these species to be warm-optimal, has led to the suggestion that global climate change and warming trends may also encourage their growth (Epstein et al. 1994).

The most widespread form of shellfish contamination by harmful marine phytoplankton is paralytic shellfish poisoning (PSP; from saxitoxin and derivatives) caused by certain dinoflagellates (Hallegraeff 1993; Table 3, Fig. 1). Other human diseases linked to toxic marine algae include diarrhetic, neurotoxic, and amnesic shellfish poisoning (DSP, from okadaic acid and other toxins; NSP, from brevetoxins; and ASP, from domoic acid, respectively; Falconer 1993*a*). These are also caused by dinoflagellates, with exception of ASP, which recently was discovered and tracked to certain benthic diatoms (Bacillariophyceae) that formerly were considered benign (*Pseudo-nitzschia* spp.; Table 2; Wright et al. 1989, Maranda et al. 1990, Fritz et al. 1992, Lundholm et al. 1994). A fourth group of poorly characterized dinoflagellate toxins, the ciguatoxins or ciguateratoxins of benthic species (e.g., *Gambierdiscus toxicus, Prorocentrum micans*), causes an array of physiological impacts to humans ranging from mild diarrhea to severe neurological dysfunction and death ("ciguatera"; Table 3; Bagnis 1993). Ciguatera finfish poisoning (CFP) is one of the most common harmful microalgae-related intoxications to humans from finfish in the world, and the only dinoflagellate-linked intoxication from finfish consumption that has been documented in the United States (Bagnis 1993). Certain marine blue-green algae (Cyanophyceae or cyanobacteria, e.g., *Trichodesmium erythraeum*) also have toxins with ciguatera-like properties (Endean et al. 1993).

Most of these algae produce endotoxins (Falconer 1993*a*) that become problematic to humans from consumption of shellfish (in PSP, DSP, NSP, and ASP) that accumulated the toxins by filter-feeding and concentrating the algae (Table 4). Higher order consumers, such as carnivorous gastropods, crustaceans (e.g., American lobster, *Homarus americanus* H. Milne Edwards 1837) and finfish (e.g., species of snapper, barracuda, grouper, and mackerel whose consumption causes CFP) can concentrate or bioaccumulate the toxins, as well, from feeding on lower order consumers (White 1981*a*, Lewis and Ruff 1993, Shumway 1995). Acute effects of most of these toxins on finfish and

TABLE 1. Currently recognized toxic estuarine and marine dinoflagellates (modified from Faust 1993, Hallegraeff 1993, Steidinger 1993, 1996, Wisessang et al. 1993, Quod 1994, Landsberg et al. 1995, Tomas 1996, Burkholder and Glasgow 1997, Matsuyama et al. 1997). (B), benthic; (P), planktonic.

Alexandrium acatenella (Whedon and Kofoid) Balech (P) (formerly *Gessnerium acatenellum, Gonyaulax acatenella, Protogonyaulax acatenella*)
A. angustitabulatum Taylor and Cassie (P)
A. catenella (Whedon and Kofoid) Balech (P) (formerly *Gessnerium catenellum, Gonyaulax catenella, Protogonyaulax catenella*)
A. cf. *cohorticula* (Balech) Balech (P) (formerly *Gessnerium cohorticula, Gonyaulax cohorticula, Protogonyaulax cohoritcula*)
A. fraterculus (Balech) Balech (P) (formerly *Gessnerium fraterculum, Gonyaulax fratercula, Protogonyaulax fratercula*)
A. fundyense Balech (P)
A. lusitanicum Balech (P)
A. minutum Halim (P) (formerly *A. ibericum, Pyrodinium minutum*)
A. monilatum (Howell) Taylor (P) (formerly *Gonyaulax monilata*)
A. ostenfeldii (Paulsen) Balech and Tangen (P) (formerly *Gessnerium ostenfeldii, Goniaulax ostenfeldii, Goniaulax tamarensis* var. *globosa, Goniodoma ostenfeldii, Gonyaulax globosa, Gonyaulax trygvei, Heteraulax ostenfeldii, Protogonyaulax globosa, Pyrodinium phoneus, Triadinium ostenfeldii*)
A. rhychocephalum Anissimowa (B)
A. tamarense (Lebour) Balech (P) (formerly *Alexandrium excavatum* [?], *Gessnerium tamarensis, Gonyaulax excavatum, G. tamarense, G. tamarensis, G. tamarensis* var. *excavata, Protogonyaulax tamarense*)
Amphidinium carterae Hurlbert (B)
A. operculatum Claparède and Lachmann (P) (formerly *A. klebsii*)
Cochylodinium polykrikoides Margelef (B) (formerly *C. heterolabatum*)
Cochylodinium sp. (P)
Coolia monotis Meunier (B) (formerly *Glenodinium monitis, Ostreopsis monotis*)
Dinophysis acuminata Claparède and Lachmann (P)
D. acuta Ehrenberg (P)
D. caudata Saville-Kent (P)
D. fortii Pavillard (P)
D. norvegica Claparède and Lachmann (P)
D. sacculus Stein (P)
D. tripos Gourret (P) (formerly *Dinophysis caudata* var. *tripos*)
Gambierdiscus toxicus Adachi and Fukuyo (B)
Gymnodinium breve Davis (P) (formerly *G. brevis, Ptychodiscus brevis*)
G. catanatum Graham (P)
G. flavum Kofoid and Swezy (P)
G. galatheaum Braarud (P)
G. mikimotoi Miyake and Kominami ex Oda (P) (formerly *G. nagasakiense*)
G. sanguineum Hirasaka (P) (formerly *G. nelsonii, G. splendens*)
G. veneficum Ballantine (P)
Gymnodinium sp. (P)
Gyrodinium aureolum Hulburt (P)
Heterocapsa circularisquama Horiguchi (P)
Lingulodinium polyedrum (Stein) Dodge (P) (formerly *Gonyaulax polyedra*; with *G. acatenella, G. monilata*)
Ostreopsis heptagona Norris, Bomber, and Balech (B)
O. lenticularis Fukuyo (B)
O. ovata Fukuyo (B)
O. mascarenensis Quod (B)
O. siamensis Schmidt (B)
Peridinium polonicum Woloszynska (P)
Pfiesteria piscicida Steidinger & Burkholder (B, P)
Pfiesteria sp. (B, P), *Pfiesteria*-like sp. (1; B, P)
Phalacroma mitra Schutt (P) (formerly *Dinophysis mitra, Prodinophysis mitra*)
P. rotundatum (Cleparède and Lachmann) Kofoid and Michener (P) (formerly *Dinophysis rotundata, Prodinophysis rotundata*)
Prorocentrum balticum (Lohmann) Loeblich III (B) (formerly *Exuviaella baltica*)
P. concavum Fukuyo (B)
P. hoffmannianum Fayst (B)
P. lima (Ehrenberg) Dodge (B) (formerly *Cryptomonas lima, Dinopyxix laevis, Exuviaella laevis, E. lima, E. marina, E. marina* var. *lima*)
P. maculosum Faust (B)
P. mexicanum Tafall (B) (formerly *P. maximum, P. rathymum*)
P. micans Ehrenberg (B)
P. minimum (Pavillard) Schiller (B) (formerly *Exuviaella mariae-lebouriae, E. minima, Prorocentrum mariae-lebouriae, P. triangulatum*)
Pyrodinium bahamense var. *compressum* (Bohm) Steidinger, Tester and Taylor (P) (formerly *Gonyaulax schilleri, Pyrodinium bahamense* var. *compressa, Pyrodinium schilleri*)
Scripsiella spp. (B)

Note: Toxicity status is uncertain for *Gambierdiscus monilata, Gymnodinium anguineum, Prorotreopsis siamensis,* and *Noctiluca scintillans.* Note that 35 species are predominantly planktonic, 20 species are predominantly benthic, and 3 species have active, common benthic and planktonic stages; that is, of the 58 known toxic dinoflagellate species, ~40% are actually benthic in habit.

shellfish are fairly well characterized, especially for brevetoxins that commonly cause massive fish kills in low densities (≥300 cells/mL; Steidinger and Baden 1984, Steidinger 1993), and for some saxitoxin-producing species that are lethal to larvae and juveniles of commercially important finfish (Robineau et al. 1991). Recently discovered toxic predatory dinoflagellates (*Pfiesteria piscicida* and at least two other *Pfiesteria*-like species) exhibit direct attack behavior toward live fish and their fresh tissues (Smith et al. 1988, Burkholder et al. 1992, Landsberg et al. 1995, Steidinger et al. 1996). They produce as yet poorly characterized lipophilic exotoxin(s) that are directly lethal to finfish and shellfish in low densities (~250–300 cells/mL; Burkholder et al. 1995*a*, Landsberg et al. 1995). Unlike most toxic dinoflagellates, which are photosynthetic, these predators are heterotrophs, although they can adopt a mixotrophic habit by retaining the chloroplasts of microalgal prey that they sometimes consume (known as kleptochloroplastidy; Lewitus et al. 1995*a*, Steidinger et al. 1995). A growing number of other dinoflagellate species also produce uncharacterized

TABLE 2. Some linkages between harmful marine microalgae, heterotrophic dinoflagellates, and anthropogenic nutrient loading to coastal waters. "Harmful" is defined as being directly or indirectly adverse to fish resources or humans (i.e., can include nontoxic as well as toxic species).

Harmful species	Link to cultural eutrophication
Chattonella antiqua	Bloomed under cumulative high loading of poorly treated sewage and other wastes, coinciding with human population growth (Japan; fish kills, toxic; Lam and Ho 1989).
Chrysochromulina polylepis	Toxic outbreaks followed change in nutrient supply ratios from cumulative increased nutrient loading (Europe; fish kills, toxic; Kaas et al. 1991, Maestrini and Granéli 1991).
Gymnodinium mikimotoi	Bloomed under cumulative high loading of poorly treated sewage and other wastes, coinciding with human population growth (Japan, as *G. nagasakiense*; fish kills, PSP; Lam and Ho 1989).
Gonyaulax polygramma Stein	Bloomed under cumulative high loading of poorly treated sewage and other wastes, coinciding with human population growth (Japan; fish kills from oxygen depletion; Lam and Ho 1989).
Noctiluca scintillans (MaCartney) Kofoid and Swezy	Bloomed under cumulative high loading of poorly treated sewage and other wastes, coinciding with human population growth (Japan; fish kills from oxygen depletion; Lam and Ho 1989).
Nodularia spumigena	Blooms followed change in nutrient supply ratios from cumulative increased nutrient loading by sewage, agricultural wastes (Baltic Sea—Rinne et al. 1981; estuary in Australia—Hillman et al. 1990).
Pfiesteria piscicida, a second toxic *Pfiesteria*-like species	Most kills [with highest cell densities] have occurred in P- and N-enriched estuaries (e.g., near phosphate mining, sewage inputs, or animal waste operations); between kill events, can prey upon flagellated algae that are stimulated by inorganic nutrients; bloomed 1 wk after a major swine effluent lagoon rupture (with extremely high phosphorus and ammonium) into an estuary, in a location where high abundance of these dinoflagellates had not been documented for at least the previous 1.5 yr; highly correlated with phytoplankton biomass in other eutrophic estuaries (mid-Atlantic and southeastern United States; fish kills, epizootics; Burkholder et al. 1995*a*, Glasgow et al. 1995, Burkholder and Glasgow 1997).
Phaeocystis spp.	Bloomed following cumulative high loading of poorly treated sewage (Europe; fish—*Phaeocystis pouchetii* [Hariot] Lagerheim); blooms were correlated with altered N/P ratios from cumulative increased nutrient loading (*P. pouchetii*; Hallegraeff 1993, Riegman et al. 1993); bloomed 1 week after a major swine effluent lagoon rupture into a eutrophic estuary (*Phaeocystis globosa* Scherffel, along with *Pfiesteria piscicida*; southeastern United States; Burkholder et al. 1996).
Prorocentrum minimum	Bloomed under cumulative high loading of poorly treated sewage and other wastes, coinciding with human population growth (Japan; fish kills, toxic; Lam and Ho 1989); blooms coincide with cumulative high loading of N from sewage, agricultural runoff, atmospheric loading, etc. (southeastern United States; Mallin 1994).
Prymnesium parvum	Toxic outbreaks usually have occurred under eutrophic conditions (fish kills; Edvardsen and Paasche 1997).
Pseudo-nitzschia multiseries, other *Pseudo-nitzschia* spp.	Have occurred with sewage and other wastes (Canada; ASP) (Smith et al. 1990); consistent seasonal blooms in the Mississippi and Atchafalya River plume areas, associated with hypereutrophic conditions (Q. Dortch et al., *unpublished data*) and in Prince Edward Island, Canada following anthropogenic nutrient loading and drought (Smith et al. 1990).†

Note: Many of the known harmful estuarine/marine microalgae also have been shown to be stimulated by N and/or P in culture, expected since they are photosynthetic (e.g., Anderson et al. 1984, 1990, Bates et al. 1991, Morlaix and Lassus 1992, Tomas and Baden 1993, Flynn and Flynn 1995, Hillebrand and Sommer 1996, Pan et al. 1996).

† But note: blooms have not been associated with eutrophic conditions in the northwestern United States (Horner and Postel 1993).

toxins that have been demonstrated to be lethal to various life history stages of finfish and shellfish (Steidinger 1993).

Members of other taxonomic divisions such as the chrysophytes (e.g., *Chrysochromulina polylepis* Manton and Parke, *Phaeocystis* spp., *Prymnesium patelliferum* Green, Hibberd and Pienaar; *Prymnesium parvum* Carter; *Chattonella antiqua* [Hada] Ono, *Chattonella marina* [Subramanyan] Hara and Chihara; *Heterosigma akashiwo* [Hada] Hada) and other blue-green algae (e.g., *Nodularia spumigena* Mertens) are potentially lethal to cultured and wild fish via exotoxin and/or endotoxin production (Sivonen et al. 1989, Maestrini and Granéli 1991, Falconer 1993*b*, Steidinger 1993) or, in some cases, by producing copious mucilage that blankets and suffocates finfish and shellfish (Savage 1932, Humm and Wicks 1980, Chang 1983, Estep and MacIntyre 1989). *C. polylepis* excretes substances that strongly irritate gill tissue and initiate mucus production, a form of "remote parasitism" (dasmotrophy, from the Greek δαομοσ, tribute or tax) since the alga consumes materials from the mucus (Estep and MacIntyre 1989). In high abundance, however, toxins from *C. polylepis* cause the fish to secrete so much mucus that death occurs from suffocation. Within the past decade, nontoxic marine algae also have proved

TABLE 3. Human exposure to toxins from marine/estuarine microalgae and heterotrophic dinoflagellates, through consumption of shellfish or finfish. Distribution on or near the North American continent is indicated in parentheses.

Type	Acronym	Distribution	Causative agent
Amnesic shellfish poisoning (domoic acid: a potent neurotransmitter, glutamate)	ASP	Cosmopolitan (Canada, Gulf and West Coasts)	Diatoms (*Pseudo-nitzschia multiseries* (Hasle) Hasle, *P. australis* Frenguelli, *P. pseudodelicatissima* Hasle, *P. seriata* Cleve, *P. delicatissima* Cleve, *Amphora coffeaeformis* Kützing [culture])
Ciguatera finfish poisoning (suite of polyethers as ciguatoxin, scaritoxin, gambiertoxin, maitotoxin, and derivatives; mostly poorly characterized)	CFP	Tropical (Southeast, Hawaii, Puerto Rico)	Dinoflagellates (*Gambierdiscus toxicus* and cohorts *Prorocentrum lima, P. concavum, P. hoffmannianum, Ostreopsis lenticularis, O. siamensis*; blue-green (*Trichodesmium erythraea* Ehrenberg)
Diarrhetic shellfish poisoning (the polyether, okadaic acid; dinophysistoxins, pectenotoxins, yessotoxins, and derivates)	DSP	Cold and warm-temperate Atlantic, Pacific, Indo-Pacific (Canada, Northeast?)	Dinoflagellates (*Dinophysis* spp., *Prorocentrum lima*)
Neurotoxic shellfish poisoning (more than nine polyether brevetoxins and derivatives)	NSP	Subtropical/warm temperate Gulf Coast, eastern Florida, North Carolina	Dinoflagellates (*Gymnodinium breve, Gymnodinium* sp.)
Paralytic shellfish poisoning ($\geq$ 18 carbamate, decarbamoyl, and sulfocarbamyl toxins and derivatives, e.g., saxitoxins, neosaxitoxins)	PSP	Cosmopolitan (Northwest, West, Northeast, Florida)	Dinoflagellates (*Alexandrium* spp., *Gymnodinium catenatum, Lingulodinium polyedrum, Pyrodinium bahamense* var. *compressum*, etc.)

Note: Modified from Maranda et al. 1990, Schulman et al. 1990, Sournia et al. 1991, Endean et al. 1993, Falconer 1993*a*, Steidinger 1993, Taylor et al. 1994, Landsberg 1996. Venerupin shellfish poisoning (VSP), from consumption of shortnecked clams (*Venerupis semidecussata* Reeve) and Pacific oysters (*Crassostrea gigas* Thunberg), is associated with *Prorocentrum minimum*. Its role in human intoxication is in debate, but it is known to be toxic to bivalve shellfish (Akiba and Hattori 1949, Okaichi and Imatomi 1979, Silva 1985).

lethal to fish and otherwise costly to fishermen by mechanisms unrelated to water column oxygen depletion (Hallegraeff 1993). For example, certain nontoxic diatoms (*Chaetoceros concavicornis* Mangin, *C. convolutus* Castracane) have extremely sharp cellular extensions that also promote capillary hemorrhage, dysfunction of gas exchange at the gills, and high mucus production and suffocation of cultured and wild salmonids (Hallegraeff 1993) as well as red king crabs (*Paralithodes camtschatica* Tilesius; Tester and Mahoney 1995). Significant economic loss can be sustained from densities as low as 10^4 cells/L (Rensel 1993). Slime accumulation from increasing growth of nontoxic algae such as the diatom *Coscinodiscus,* or the chrysophytes *Phaeocystis* spp., during some periods have been sufficiently heavy to clog or rip fishermen's nets (e.g., Chang 1983, Lancelot et al. 1987, Cherfas 1990). The chrysophyte "brown tide" algae, *Aureococcus anophagefferens* Sieburth, Johnson, and Hargraves (New England) and *Aureoumbra lagunensis* (gen. et sp. nov.; H. DeYoe and coworkers, Laguna Madre, Gulf Coast; P. Hargraves, URI) are poorly consumed by microcrustacean zooplankton or larval fish species, but mortality increases after a threshold density of brown tide cells is attained (Buskey and Stockwell 1993, Whitledge 1993).

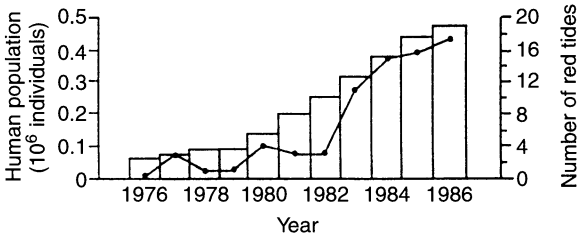

FIG. 1. Observed correlation between the number of red tide outbreaks per year in Tolo Harbor (continous line) and the increase in human population of Hong Kong (bars) during 1976–1986 (Lam and Ho 1989; from Hallegraeff 1993).

Direct parasitism by nontoxic marine dinoflagellates represents another widespread mechanism of fish death (Cachon and Cachon 1987, Love et al. 1993). Diverse parasitic dinoflagellate species are abundant and cosmopolitan, but their cryptic behavior and complex life cycles render them difficult to characterize and, often, even difficult to detect or diagnose (Cachon and Cachon 1987). They have been identified, nonetheless, as causative agents of mass mortalities in finfish and shellfish (Hollande and Cachon 1953, Cachon and Cachon 1987, Lom and Dykova 1992, Love et al. 1993, Noga 1993). For example, the parasite *Ichthyodinium chabelsrdi* Hollande and Cachon has caused mass mortality of sardines in the Mediterranean (Hollande and Cachon 1953, Cachon and Cachon 1987). *Amyloodinium ocellatum* is a virulent pathogen that parasitizes warm-water estuarine and marine finfish such as cultured and

TABLE 4. Examples of known chronic or sublethal, direct, and indirect impacts of harmful estuarine/marine phytoplankton and heterotrophic dinoflagellates on finfish and shellfish (adult animals unless otherwise specified) and their associated food webs.

Impact	Causative agent	Affected species
Native finfish		
Narcosis (lethargy, sometimes prolonged)	*Pfiesteria piscicida*	Various species (e.g., Atlantic croaker, Atlantic menhaden, red drum, southern flounder, striped bass (Burkholder et al. 1995*a*)
Impaired swimming behavior, loss of balance; loss of appetite; enhanced vulnerability to predators	*Gymnodinium breve*	Various species (Steidinger and Baden 1984)
	Alexandrium spp., *Gonyaulax polyedra*	Various species (White 1981*b*)
	Pfiesteria piscicida	Various species (Burkholder et al. 1995*a*)
	Gambierdiscus toxicus	Various species (reviewed in Landsberg 1995)
Hyperplasia, hypertrophy fusion of secondary lamellae	*Chaetoceros concavicornis*	Salmonids (reviewed in Bruslé 1995)
Mucus production leading to suffocation	*Chaetoceros concavicornis*	Chinook salmon (Rensel 1992, Yang and Albright 1994)
Necrosis and sloughing of gill lamellae	*Distephanus speculum* Ehrenberg	Atlantic salmon (Bruno et al. 1989)
Loss of selective cell permeability in gill	*Prymnesium parvum, Chrysochromulina polylepis*	Various finfish and shellfish (Ulitzur and Shilo 1966, Underdal et al. 1989)
Edema and degenerative change of the epithelium	*Heterosigma akashiwo*	Chinook salmon (Chang et al. 1990)
Pathological changes in gill tissue; depressed heart rate and reduced blood circulation	*Chattonella marina, C. antiqua*	Yellowtail, red sea bream, carp (Endo et al. 1992, Toyoshima et al. 1989)
Depressed white blood cell count, diffuse splenic lymphoid depletion, other changes suggestive of a thrombocytopenia and lymphopenia; severely increased osmolality	*Pfiesteria piscicida*	Striped bass, southern flounder (Noga et al. 1996; E. J. Noga, *unpublished data*; H. B. Glasgow and J. M. Burkholder, *unpublished data*)
Pathological changes in gill, liver, and intestines; blanching of skin	*Gambierdiscus toxiccus*	Various species (reviewed in Landsberg 1995)
Hepatic disease	Blue-greens (microcystin from feed)	Cultured Atlantic salmon (Andersen et al. 1993)
Ulcerative diseases (weeks to months, sometimes coinciding with reproductive periods)	*Pfiesteria piscicida*, second *Pfiesteria*-like species	Atlantic menhaden (Burkholder et al. 1992, 1995*a*, Noga et al. 1996); also observed during field epizootic affecting Atlantic field epizootic affecting Atlantic menhaden, American eel, Atlantic croaker, pinfish, red drum, river herring, southern flounder, striped bass, white perch (Burkholder et al. 1995*a*, Burkholder and Glasgow 1997)
Loss of egg viability	Parasitic dinoflagellate spp.	Various species (Cachon and Cachon 1987)
	Pfiesteria piscicida	Atlantic menhaden (Burkholder et al. 1995*a*)
Gastrointestinal, respiratory, and reproductive diseases	Parasitic dinoflagellates, e.g., *Amyloodinium ocellatum* (Brown) Brown and Horasse	Various species (Lom and Dykova 1992, Noga 1993)
Native shellfish		
Narcosis (prolonged lethargy, reduced fright response and/or reduced shell valve closure, reduced burrowing)	*Alexandrium* spp.	Various bivalve mollusks (Bricelji et al. 1987, Shumway and Cucci 1987)
	Pfiesteria piscicida	Bay scallop, eastern oyster (pediveligers), blue crab, northern quahog (Burkholder et al. 1995*a*)
	Gymnodinium breve	Bay scallops, surf clams, oysters, southern quahogs, coquinas (Falconer 1993*a*, Steidinger 1993)
Depressed or altered feeding	*Alexandrium* spp.	Various mollusk spp. (Shumway and Cucci 1987)
	Alexandrium tamarense	Pacific oyster (Lassus et al. 1996)
	Pfiesteria piscicida	Shellfish spp. (as above; Burkholder et al. 1995*a*)
	Gyrodinium aureolum	Scallops (Lassus and Berthome 1988), mussels (Widdows et al. 1979)
Decreased activity of lateral cilia (apparently via a dopaminemimetic substance)	*Aureococcus anophagefferens*	Various bivalve mollusks (Gainey and Shumway 1991)
Increased mucus production	*Alexandrium* spp.	Mollusk species (Shumway and Cucci 1987)

TABLE 4. Continued.

Impact	Causative agent	Affected species
Haemocyte abnormalities	*Pseudo-nitzschia pungens* f. *multiseries*	Pacific oyster (Jones et al. 1995)
Poor shell growth	*Prorocentrum minimum, Chrysochromulina polylepis*	Eastern oyster (Luckenbach et al. 1993), Mussels (Nielsen and Strømgren 1991)
Depressed general growth	*Gyrodinium aureolum*	Mussels (Widdows et al. 1979)
Shell disease	*Pfiesteria piscicida*	Blue crab (H. B. Glasgow and J. M. Burkholder, *unpublished data*)
Inhibition of feeding; poorly developed digestive diverticula; attenuation of the epithelium–abnormal vacuolation, necrosis; large thrombi (heart, open vascular system of mantle, digestive diverticula, gill, kidney)	*Prorocentrum minimum*	Bay scallop, eastern oyster (Wikfors and Smolowitz 1993)
Disseminated neoplasia, germinomas	*Alexandrium* spp., other PSP dinoflagellates	Softshell clam, northern quahog, blue mussel, cockle, other sensitive species
Neoplasia (hematopoietic system)	*Prorocentrum minimum*	Oysters, other sensitive species (reviewed in Landsberg 1996; hypothesized from strong correlative data)
Mantle and gill lesions;	*Gyrodinium aureolum*	Eastern oyster (juveniles; Smolowitz and Shumway 1996);
Decreased absorptive cell height, increased lumen diameter		Bay scallop (juveniles; Smolowitz and Shumway 1996)
Blood, gastrointestinal, and reproductive diseases	Parasitic dinoflagellate spp. (e.g., *Hematodinium perezi* Chatton and Poisson)	Various decapod crustaceans (Cachon and Cachon 1987, Love et al. 1993, Shields 1994)
Increased protozoan (kidney) and bacterial (urinary space) infections	*Gyrodinium aureolum*	Bay scallop (Smolowitz and Shumway 1996)
Improper settling	*Pfiesteria piscicida*	Eastern oyster (pediveligers; Burkholder et al. 1995*a*)
Recruitment failure	*Gymnodinium breve*	Bay scallop (Summerson and Peterson 1990)
Impaired recruitment timing	*Aureococcus anophagefferens*	Bay scallop (Tettelbach and Wenczel 1993)
Reduced reproduction and early development	*Chrysochromulina polylepis*	Mussels (Granmo et al. 1988)
Food resources and habitat		
Reduced fecundity of zooplankton (egg production, viability)	*Chrysochromulina polylepis; Pfiesteria piscicida*	Microcrustaceans (e.g., *Acartia, Temora, Centropages*), ciliates (Skjoldal and Dundas 1991); Rotifers (after 7 d; Mallin et al. 1995)
Reduced fecundity of zooplankton (egg production, viability)	*Pseudonitzschia pungens, Aureococcus anophagefferens*	Rotifers (after 5 d; Whyte et al. 1996); Microcrustaceans (Smayda and Villareal 1989), Busky and Stockwell 1993, Lonsdale et al. 1996)
Castration and feminization	Parasitic dinoflagellates spp. (e.g., *Hematodinium, Blastodinium*)	Microcrustaceans, ciliates (Cachon and Cachon 1987)
Mortality of zooplankton and other microfauna	*Chattonella marina*	Microcrustaceans (Tomas 1981), tintinnids (Verity and Stoecker 1982)
Mortality of phytoplankton	*Chrysochromulina polylepis*	Dinoflagellate (*Heterocapsa*) (Moestrup and Arlstad 1993)
Reduced growth of microflora and microfauna	*Chrysochromulina polylepis*	Diatoms (Mykelstad et al. 1995), ciliates (Carlsson et al. 1990), heliozoans (Tobiesen 1991)
Reduced microfauna feeding	*Chrysochromulina polylepis; Nodularia spumigena, Aphanizomenon* cf. *flosaquae*	Ciliates (Carlsson et al. 1990); Microcrustaceans (Sellner et al. 1996)
Increased viscosity of water, with impaired breathing;	*Phaeocystis pouchetii, P. globosa*	Various finfish and shellfish species (Pieters et al. 1980, Chang 1983, Lancelot et al. 1987, Riegman and van Boekel 1996);
Altered migration path		Herrings (Savage 1932)
Clogging of the gills, breathing impairment	*Trichodesmium erythraeum*	Sharks (Humm and Wicks 1980)
Anoxia/hypoxia†	*Ceratium tripos* (O. F. Müller) Nitzsch, *Gymnodinium sanguineum, Gonyaulax polygramma* Stein, *Noctiluca scintillans* (MaCartney) Kofoid & Swezey, *Trichodesmium erythraeum*	Various finfish and/or shellfish species (Mahoney and Steimle 1979, Mijares et al. 1985, Harper and Guillen 1989, Lam and Yip 1990, Hallegraeff 1993)

TABLE 4. Continued.

Impact	Causative agent	Affected species
Loss of seagrass habitat from severe light reduction†	*Aureococcus anophagefferens, Aureodoris lagunensis*	Eelgrass (*Zostera marina* L.; Dennison et al. 1989), shoalgrass (*Halodule wrightii* Ashers; Dunton 1994)

Notes: Species names for finfish and shellfish that were not included in prior text are given as American eel (*Anguilla rostrata* Lesueur), Atlantic croaker (*Micropogonias undulatus* L.), Atlantic salmon (*Salmo salar* L.), blueback (river) herring (*Alosa aestivalis* L.), carp (*Cyprinus carpio* L.), chinook salmon (*Oncorhynchus tschawitscha* L.), eastern oyster (*Crassostrea virginica* Gmelin), northern quahog (*Mercenaria mercenaria* Linne), pinfish (*Lagodon rhomboides* L.), red sea bream (*Pagrus major* Temminck and Schegal), southern flounder (*Paralichthys lethostigma* Jordan and Gilbert), striped bass (*Morone saxatilis* Walbaum), white perch (*Morone americana* Gmelin), and yellowtail (*Seriola quinqueradiata* Temminck and Schegal).

† These events were also lethal to many fish.

wild striped bass (Lom and Dykova 1992, Noga 1993). In coastal Alaska, *Hematodinium* sp. has caused increasing concern since the mid-1980s for its role in "bitter crab" disease. The pathogen infects tanner crabs (*Chionoecetes bairdi* Rathbun 1924) during their molt; once established, it is 100% lethal, and the meat becomes unmarketable before the crabs die (Love et al. 1993). Little is known about natural controls or environmental factors that favor these parasites during periods in their life cycles when they are not associated with fish hosts (Lom and Dykova 1992).

The Emerging Issue of Sublethal/Chronic Impacts

Impacts to fish populations from harmful marine microalgae and heterotrophic dinoflagellates have been considered primarily from the limited view of acute or lethal influence (White 1981*a*, Falconer 1993*a*). Although shellfish traditionally have been regarded as unaffected "vectors" in outbreaks of toxic marine phytoplankton, amassing evidence indicates that chronic and/or sublethal impacts of these toxins are both serious and extensive to a wide array of shellfish (Shumway 1995, Anderson 1995, Landsberg 1996; Table 4). Removal (mortality) of parental stocks by a toxic red tide (*Gymnodinium breve*) was identified as the mechanism for recruitment failure of natural populations of bay scallops (Summerson and Peterson 1990). Similarly, blooms of the brown tide species *A. anophagefferens* have been correlated with poor recruitment of juvenile bay scallops and slow recovery of scallop stocks (Tettelbach and Wenczel 1993), possibly through stimulation of gamete resorption in reproductive adults, failure and/or delay of larval settlement and metamorphosis, mortality of early life-history stages, and/or reduced growth of juveniles. Copious mucus production by *Phaeocystis* spp. has been shown to impair gill functioning in wild fish stocks (Pieters et al. 1980, Chang 1983). Bioaccumulation of saxitoxins and ciguatoxins, with depressed survival and recruitment, has been demonstrated experimentally for larval and adult finfish (White 1981*a*, *b*, Steidinger and Baden 1984, Robineau et al. 1991). This mechanism has been implicated in reducing viability of finfish at the population level, leading to overall impairment of food web structure and function (Robineau et al. 1991, Landsberg 1995).

Recent research suggests a potential chronic role of ciguatoxins in causing disease and reducing long-term survival of reef finfishes (Landsberg 1995; Fig. 2). Ciguatoxins are neurotoxic, hemolytic, and/or hemoagglutinating (Table 4). They can be lipid- or water-soluble, are regarded as the most widespread and least understood of the dinoflagellate toxins, and induce an array of adverse chronic health effects for humans that may have some analogies for fish (Russell and Egen 1991; Tables 4 and 5). On the basis of reports from physicians in the Orient, the Caribbean, the South Pacific, and Australia, the number of human cases of CFP is underestimated by half on an annual basis (Hokama and Miyahara 1986). Much less is known about impacts on aquatic organisms, since studies on fish poisoning where death is not a sequel are subject to high variation and difficulties in detection/diagnosis. It has been hypothesized that long-term impacts of CFP on humans may represent an immune sensitization phenomenon. Polycyclic ether ciguateratoxins react with specific T-lymphocytes in producing abnormal immunoglobulin E that, in turn, fixes onto mast cells to inhibit granule release of serotonin (Hokama and Miyahara 1986). Ingestion of the ciguatoxin producer, *Gambierdiscus toxicus,* or ciguatera-contaminated tissues, have been shown experimentally to induce pathology in fish gills, liver, and intestine (Capra et al. 1988, Gonzalez et al. 1994), as well as behavioral changes (disorientation, loss of equilibrium, depressed feeding; Kelley et al. 1992, Magnelia et al. 1992). Landsberg (1995) invoked the potential for immune system suppression and other general physiological impairment in hypothesizing that ciguatera toxins enable opportunistic bacteria and fungi to cause epizootics in reef fishes that consume macroalgae colonized by *G. toxicus* (Fig. 2).

Potential ciguatoxin contributors include at least one blue-green algal species, *Trichodesmium erythraeum,* as previously mentioned, but little information is available about the role of this organism or other cyanophytes in ciguatera-related fish diseases. Direct chronic impacts on finfish from the blue-green alga *Nodularia spumigena,* through production of the hepatotoxin, nodularin, are better understood (Table 4). Nodularin, a

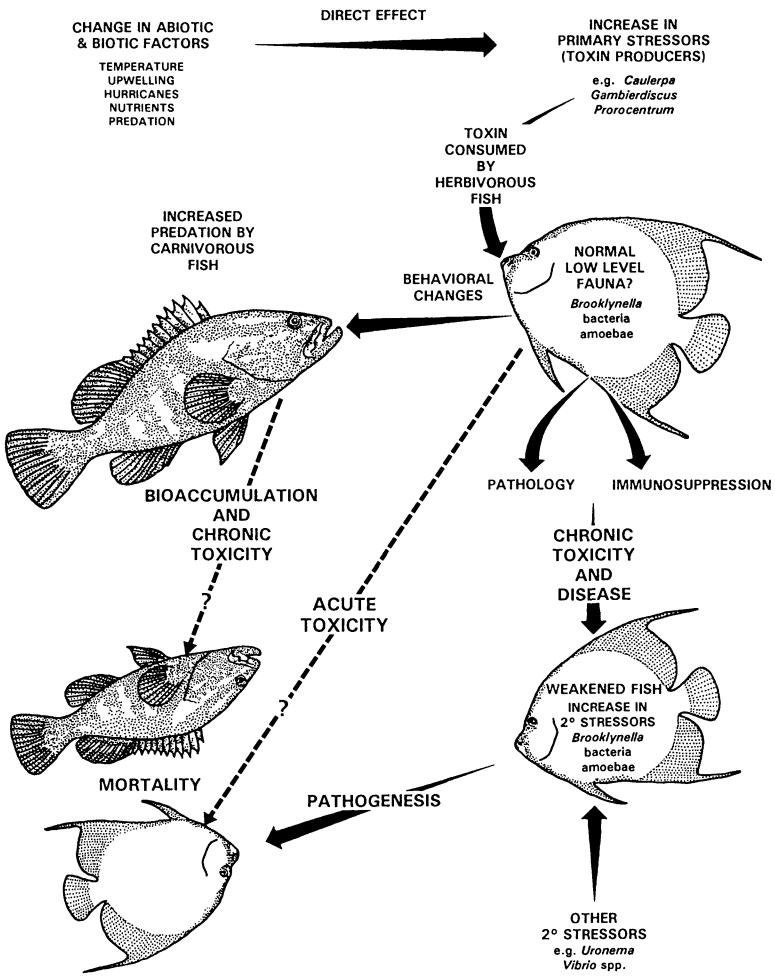

FIG. 2. Food web hypothesis for the observed series of events in the Florida reef fish kills, indicating major primary and secondary stressors including chronic behavioral changes, pathology, and immunosuppression (from Landsberg 1995).

cyclic pentapeptide toxin, inhibits protein phosphatases 1 and 2A, which can promote cytoskeletal disintegration, tissue injury, and tumor development at chronic levels (Runnegar et al. 1988, Falconer 1993*b*). Protein phosphatases are characteristic of eukaryotes, so that both competing autotrophic eukaryotes and grazing eukaryotes, as well as fish, potentially could be inhibited (Falconer 1993*b*). Nodularin can be accumulated by shellfish; for example, highly toxic edible mussels (*Mytilus edulis* Gould 1850) were found in an estuary during a bloom of *N. spumigena* (Falconer et al. 1992). However, direct chronic effects of these toxins on finfish and shellfish are, as yet, poorly documented. Toxic freshwater blue-green algae also have been observed in coastal waters and embayments, sometimes in bloom densities, and likely derived from fluvial discharge since they generally are known to be poor osmoregulators (e.g., *Anabaena* spp., *Microcystis aeruginosa, Oscillatoria* sp.; Niemi 1988, Kononen and Sellner 1995). Some of these toxins, such as microcystin, have been traced to commercially produced feed for cultured fish (Anderson et al. 1993) and potentially could persist for extended periods (W. Carmichael, *personal communication*), but their impacts on estuarine and marine fish populations are not known.

In the past 25 yr, there has been an increase in the frequency of two major types of cancer in bivalves that cause debilitation as well as mortality in shellfish stocks (Landsberg 1996). Disseminated neoplasia affects ~15 species worldwide, and is common in softshell clams (*Mya arenaria* L.), cockles (*Cerastoderma edule* L.), and blue mussels (*Mytilus edulis*). In softshell clams, observations of up to ~80% mortality from disseminated neoplasia suggest that this disease significantly contributes to recent population declines in New England and Chesapeake Bay (Brousseau and Baglivo 1991). Pathogenesis is similar to that of vertebrate leukemia in that the circulating tumor cells rapidly divide, ultimately invade the connective tissue, and then kill the host (Miosky et al. 1989). In some affected

TABLE 5. Known chronic/sublethal impacts to mammals that can occur from toxic estuarine and marine microalgae and heterotrophic dinoflagellates. Poisoning refers to the listed toxins and their derivatives.

Poisoning	Agent(s)	Effects
Brevetoxins (NSP)	*Gymnodinium breve*	Cause substantial and persistent depolarization of nerve membranes. Induce a channel-mediated sodium ion influx; depolarize muscle fiber membrane, and depress acetylcholine-induced depolarization. Induce differential release of neurotransmitters from cortical synaptosomes. Promote central nervous dysfunction (e.g., muscle paralysis), nausea, vomiting, diarrhea, asthma-like symptoms, susceptibility to infections†; pneumonia-like symptoms (humans, rats, mice, and manatees‡; Baden and Trainer 1993, Baden et al. 1997).
Ciguatera toxins (CFP)	*Gambierdiscus toxicus*§	Open sodium channels at resting potential, and prevent open channels from being inactivated during subsequent depolarization. Replace calcium ions at sites on neuroreceptors that control sodium permeability. Can cause calcium ion-dependent contraction in smooth and skeletal muscle tissues; can promote release of norepinephrine and dopamine from pheochromocytoma cells. Immunogenic after coupling to serum protein†; cause peripheral (CFP) nervous system dysfunction, sensitivity to alcohol; stimulate hormone and neurotransmitter release (target a ubiquitous membrane component); activate protein kinases; cause joint pain, miosis, erethism, cyanosis, prostration, nausea, vomiting, diarrhea, low blood pressure, bradycardia (humans, rats, mice; Hokama and Miyahara 1986, Baden and Trainer 1993, Bagnis 1993, Yasumoto and Murata 1993).
Domoic acid (ASP)	*Pseudo-nitzschia* spp.§	Glutamate agonist displaying neurotoxic properties in the central nervous system; causes increased firing of neurons (highest affinity of all known kainic acid analogues), permanent short-term memory loss, vomiting, nausea, severe headaches, diarrhea, muscle cramping, disorientation, hypoactivity, sedation—akinesia, rigidity, sterotype, loss of posteral control, convulsions (humans, rats, mice; Hampson and Wenthold 1988, Tasker et al. 1991, Baden and Trainer 1993).
Okadaic acid (DSP)	*Dinophysis fortii, Prorocentrum concavum, Prorocentrum concavum, P. lima, P. minimum*	Suppresses interleukin-1 synthesis in peripheral blood monocytes.† Inhibits protein phosphatase (acts on enzymes as a non-competitive or mixed inhibitor; induces hyperphosphorylation of a protein in primary [human] fibroblasts). Causes necrosis of the hippocampal region of the brain. Nonphorbol ester-type tumor promoter; blocks protein synthesis reticulocyte lysates; inhibits T-antigen stimulated DNA replication; mimics stimulation of glucose transport into adipocytes by insulin; increases production of prostaglandin E2 in peritoneal macrophages; induces ornithine decarboxylase activity following epithelial exposure (humans, rats, mice; Fujiki et al. 1987, Haystead et al. 1989, Ohuchi et al. 1989, Redpath and Proud 1989, Lawson et al. 1990, Hokama 1991, Aune and Yndestad 1993, Baden and Trainer 1993, Yasumoto and Murata 1993).
Saxitoxins (PSP)	*Alexandrium* spp., *Gymnodinium catenatum, Lingulodinium polyedra, Pyrodinium bahamense* var. *compressum*	Bind specifically to the voltage-sensitive sodium channel and block sodium ion influx in neurons. Relax vascular smooth muscle; depress rate of rise and amplitude of action potential of cardiac muscle. Cause peripheral nervous system dysfunction, nausea, vomiting, central nervous system dysfunction, malaria-like symptoms (humans, rats, mice; reviewed in Kao 1993; Baden and Trainer 1993).
Unknown toxins	*Pfiesteria piscicida*, second *Pfiesteria*-like species§	Linked to symptoms such as easy infections and depressed T4 cell densities,† respiratory illnesses and asthma-like symptoms; elevated hepatic enzyme activities; reversible cognitive impairment and short-term memory loss sustained by humans exposed to

TABLE 5. Continued.

Poisoning	Agent(s)	Effects
		aerosols from toxic cultures (Glasgow et al. 1995); profound learning disabilities and memory loss in humans exposed to water or overlying air in toxic outbreak sites (Morris et al. 1997); crude toxin preparation causes severe cognitive impairment and memory dysfunction in laboratory rats, apparently reversible after weeks (ongoing experiments, with chronic exposure trials underway, Levin et al. 1997; purified water-soluble toxin damages neuroblastoma and pituitary cells of rat tissues, J. Ramsdell and P. Moeller, *unpublished data*).
Nodularin	*Nodularia spumigena*	Promotes perchronic neurotoxicoese, gastrointestinal disturbances, cutaneous or respiratory irritation; active liver injury and elevated alanine aminotransferase in the plasma; hepatocyte necrosis; and endocyte injury. Highly specific inhibitor of dephosphorylation by protein phosphophatases 1, 2A, resulting in accumulation of tumor-promoting substances (liver, bronchogenic, abdominal carcinomas; uterine adenocarcinomas; thoracic lymphosarcomas) (mice, rats, humans; Falconer et al. 1988, Beasley et al. 1989; considered analogous to microcystin in chronic effects; Falconer 1993*b*, Ohta et al. 1994).
Lyngbyatoxin A, Aplysiatoxins, Debromoaplysiatoxin	*Lyngbya majuscula* Harvey (blue-green or cyanobacterium)	Cause skin irritation, erythema, blisters, and deep desquamation (humans); promotes tumors (rats, mice); induce differentiation of promoyelocytic leukemia cells, aggregation of lymphoblastoid cells, and stimulation of prostaglandin production and choline turnover (humans; Fujiki et al. 1984, 1985).‖
Unknown toxins¶	*Chrysochromulina polylepis, Prymnesium parvum, P. patelliferum*	Alter cell membrane permeability and ion balance; lyse erythrocytes (humans); inhibit uptake of neurotransmitters into synaptosomes of brain (rats, mice); hemolytic, hepatotoxic (rats, mice; Edvardsen et al. 1990, Yasumoto et al. 1990, Meldahl et al. 1994).

† Suggests or demonstrates immune system impairment.

‡ The manatees eventually died of pneumonia (following an 18-mo red tide event, the longest known for *G. breve*; Landsberg and Steidinger 1997), but during autopsy, brevetoxins apparently were localized in phagocytic cells (Baden 1997) that were sufficiently depleted to allow attack by bacterial pathogens.

§ Several other benthic dinoflagellates (mainly from the genera *Amphidinium, Coolia, Ostreopsis,* and *Prorocentrum,* and their associated bacterial flora) may also contribute to ciguatera poisoning (Tindall et al. 1984, Tosteson et al. 1986). The blue-green alga *Trichodesmium erythraeum* is known to produce ciguatera-like toxins, as well. See Tables 1 and 3, respectively, for toxic *Alexandrium* and *Pseudo-nitzschia* spp. listings; note that *Amphora coffeaeformis* is also an agent of ASP, but thus far has been found to be toxic only in a laboratory setting (Maranda et al. 1990). Okadaic acid is one of several toxins that cause DSP. A second species within the genus *Pfiesteria* is known to kill fish in a laboratory setting (Landsberg et al. 1995); its impacts on mammals have not yet been examined.

‖ Other marine cyanobacteria (e.g., *Schizothrix calcicola* [Ag.] Gom.—produces debromoaphysiatoxin), *Oscillatoria nigroviridis* Thwaites—produces oscillatoxin A; Carmichael et al. 1985) may also be implicated in chronic or sublethal toxicity impacts.

¶ *P. parvum* toxins are acidic polar lipids, resembling proteolipids (Carmichael et al. 1985). They are known to include at least two hemolytic glycolipids (as well as four other hemolytic substances) and two closely related polyhydroxy polyene-polyethers (Igarashi et al. 1995). The toxins of *C. polylepis* include hepatotoxic lipid extracts (Underdal et al. 1989) and hemolytic substances (Edvardsen et al. 1990). Recent work by Meldahl et al. (1994) suggests that the toxins from *C. polylepis, P. parvum,* and *P. patelliferum* are similar, although activities vary.

bivalve species, the incidence of disseminated neoplasia strongly parallels outbreaks of PSP from *Alexandrium tamarense, A. minutum, A. fundyense,* and *A. catenella,* which contain relatively high proportions of gonyautotoxin derivatives GTX1 and GTX4 (>20 molar percent; Landsberg 1996). High levels of these highly toxic carbamate gonyautoxins are also found in the tissues of affected shellfish. Softshell clams were found to have an average whole-body toxin load of ~2100 μg saxitoxin (STX) equivalents/100 g tissue (Martin et al. 1990), information that is germaine from a human health perspective in shellfish consumption. However, vital organs of exposed animals contained ~6500–10 000 μg STX equivalents/100 g tissue (in the digestive gland, heart, kidney, and brown gland).

A second common type of bivalve cancer, germinomas (gonadal tumors), is known to affect ≥10 shellfish species and one hybrid (Landsberg 1996). As for disseminated neoplasia, the epizootiology of this disease in softshell clams has been correlated with the distribution of blooms of dinoflagellates associated with PSP (*Alexandrium* spp.) and venerupin shellfish

poisoning (VSP; *Prorocentrum minimum*) following a 2–3 wk lag period. The noted correlations were conservative because they reflected only coincidences of acute bloom formation and high concentrations of toxins in bivalves. Thus, the potential effects of long-term exposures to low levels of toxin from smaller dinoflagellate populations were not examined.

Detrimental effects of dinoflagellates and their toxins on bivalve shellfish have only recently been considered (Shumway and Cucci 1987, Shumway 1990, Shumway et al. 1990, Wikfors and Smolowitz 1993, 1995). Effects of chronic exposures have not been examined. Research has focused on dinoflagellates that produce toxins that are lethal or deleterious to mammals. But recent evidence has established that dinoflagellates that are, apparently, nontoxic to mammals may be pathogenic to bivalves (e.g., *P. minimum*; Okaichi and Imatomi 1979, Taylor 1984, Wikfors and Smolowitz 1995). *P. minimum* blooms are common in many parts of the world and often are correlated with anthropogenic nutrient loading (e.g, the Albemarle-Pamlico and New River estuaries in the southeastern United States; Mallin 1994). In Chesapeake Bay, these blooms have been associated with shellfish mortalities (Luckenbach et al. 1993). Recently, pathological effects (poorly developed digestive diverticula; attenuation of the epithelium with abnormal vacuolation and necrosis; large thrombi in the heart and in the open vascular system of the mantle, digestive diverticula, gill, and kidney tissues) and feeding inhibition were experimentally demonstrated for bay scallops (*Argopecten irradians* L.; Wikfors and Smolowitz 1993, 1995).

Beyond direct toxic, sublethal chronic effects, more insidious effects of toxic dinoflagellates and chrysophytes, harmful brown tide organisms, estuarine/marine blue-green algae, and parasitic dinoflagellates have been documented on fish prey, and also on fish recruitment, reproduction, and immune system function (Table 4). The effects on target animals are highly species specific, but review of the available data points to an emerging trend of significant, pervasive impacts of sublethal levels of these microorganisms on finfish and shellfish physiology, disease resistance, growth, and reproductive success. A glimpse of the breadth of these impacts is afforded by studies on the community response of the apparently nontoxic brown tide alga, *Aureococcus anophagefferens*. The cell surface of this organism contains a bioactive substance that has been likened to dopamine (Anderson 1995). This substance interferes with ciliary beat and, thus, reduces feeding activity of filter-feeding shellfish. Egg hatching success of red and black drum (*Sciaenops ocellatus* L. and *Pogonias cromis* L., respectively) is depressed in the presence of high concentrations of *A. anophagefferens*. Significant declines in abundances of zooplankton, shellfish, and other benthic filter feeders, as well as certain commercially important finfish have been recorded (Whitledge and Pulich 1991, Busky and Stockwell 1993, Anderson 1995). Loss of sea-grass habitat from brown tide formers *A. anophagefferens* and *Aureoumbra lagunensis* also has been documented, resulting from severe shading (Dennison et al. 1989, Dunton 1994). Such effects likely have long-term consequences for year class strength and persistence of finfish and shellfish species (Anderson 1995)—consequences that, thus far, have eluded us in considerations for developing reliable predictions toward management of sustainable fisheries (National Research Council 1994). Available evidence indicates, moreover, that sublethal/chronic impacts from harmful marine microalgae and heterotrophic dinoflagellates may be expected to extend beyond finfish and shellfish to higher trophic levels such as mammals (Table 5), which would directly or indirectly affect fish through trophic interactions.

Management Response to Harmful Marine Microalgae

A clear anthropocentric focus historically has guided development of management strategies in confronting outbreaks of harmful marine microalgae and heterotrophic dinoflagellates. Successful models have not yet been developed to predict the behavior and growth of most harmful marine microalgae (Anderson 1995). Hence, management generally has focused on attempts to mitigate the impacts by preventing sickness and death in humans. Formal, although limited, monitoring programs for detection of known harmful species and toxin levels in shellfish tissues have been established at local and national levels in many countries. As a result, detection of PSP, NSP, and more recently, DSP and ASP has enabled banning of shellfish consumption when necessary (Falconer 1993*a*). But structured monitoring networks at regional geographical scales are mostly lacking (Falconer 1993*a*, Shumway et al. 1995). Management strategies for CFP must, of necessity, be more primitive because the wide suite of lipid and water-soluble ciguatera toxins have precluded development of a standard, generally applicable assay for detection (Bagnis 1993, Sullivan 1993). Marketing of certain fish species is restricted during seasons when ciguatera outbreaks are expected, and efforts are made to post areas to warn local citizens and tourists against consuming fish with the highest probability of ciguatera toxin bioaccumulation (Bagnis 1993).

The extent to which management takes the fundamental step of acknowledging linkages among harmful microalgae, shellfish contamination, fish kills, and human health impacts has been, in many instances, largely constrained by political dictates (e.g., Hallegraeff et al. 1990, Burkholder et al. 1995*a*). Because of the economic "halo" (misinformed public panic) effects on fishermen, restaurants, and coastal tourism that often accompany red tides and outbreaks of other harmful

TABLE 6. Reaction to newly discovered harmful marine microalgae (Wright et al 1989, Anonymous 1991, Burkholder et al. 1992, 1995*a*, Cembella and Todd 1993, Horner and Postel 1993, Glasgow et al. 1995, Barker 1997).

Factor	*Pseudo-nitzschia*	*Pfiesteria*
Toxin(s)	Domoic acid (relatively easy detection)	Unknown toxins (verified but not yet identified)
Unusual features	Origin (diatom)	Exotoxins (water, aerosols); complex life cycle and behavior
First known target	≥107 humans (1987); 3 deaths	Fish (10^3–10^9, massive kills, epizootics; 1991)
Human exposure	Shellfish poisoning (ASP)	Water contact, aerosol inhalation (laboratory setting; anecdotal evidence from fish kill sites)
Symptoms (humans)	Permanent "Alzheimer's-like" short-term memory loss, suite of other symptoms sometimes leading to death	Not recognized/not related (for 4 yr); reversible short- and long-term memory loss, suite of other symptoms; not yet known to be lethal
Symptom detection	Acute, obvious	Insidious, ± time lag factor
Status of science	Accepted (Canadian Government research scientists)	Impacts to fish or humans were rejected by state officials for >5 yr despite corroboration and referred publications
Overall regulatory response	Canada: Cooperation, United States (California, the Northwest): Cooperation	United States (North Carolina)—High, sustained resistance, United States (Maryland and Delaware)—Cooperation

algae (Steidinger and Baden 1984, Diaby 1996), regulators and scientists confront strong political forces whose general motivation is to downplay the impacts of these organisms and attribute their outbreaks to natural rather than anthropogenic factors. In some cases, such as toxic outbreaks by known PSP and NSP dinoflagellates, the risks of death and serious illness in humans from shellfish consumption have been so thoroughly documented that the agency must err on the side of caution in prohibiting shellfish harvest (Falconer 1993*a*). But, when the toxins are poorly characterized and impacts to human health are not conclusively related to shellfish harvest, political and economic concerns generally limit management response even for human health protection. Therefore, it is logical to expect that development of management strategies that address acute or chronic impacts of harmful marine microalgae to finfish and shellfish historically have been given low priority in management considerations.

Newly discovered harmful microalgae present a greater challenge to scientists in communicating with state and federal regulators. The following two case histories illustrate the spectrum in management response (Table 6). In 1987, neurological intoxication of >100 people, with several deaths, led the Canadian government to seek out experts in organic chemistry and toxicology among government scientists, who were given all the facilities they requested to track and diagnose the problem (Wright et al. 1989). After three days, the illnesses were traced to consumption of blue mussels. The guts of these shellfish were packed with diatoms of the species *Pseudo-nitzschia pungens* f. *multiseries,* which had been known as a naturally occurring benign component of the marine flora for several decades. The mussel tissues and the diatoms contained a toxin that was identified within five days as domoic acid. This was the first known record of a diatom producing toxin, and the first known record of a harmful marine microalga with domoic acid—the substance previously had been found only from certain red macroalgae (*Chondria armata* Okam., *C. baileyana* [Montagne] Harvey, and *Alsidium* sp.; Takemoto and Daigo 1958, Impellizzeria et al. 1975). Despite the novelty of the situation, the Canadian government immediately accepted the findings, designed and implemented an extensive ongoing federal monitoring program, and completed a detailed analysis of effects.

Four years later in 1991, toxic *Pseudo-nitzschia* involvement was suspected by a veterinarian in the death of pelicans from Monterey Bay, California. The guts of the anchovies that the pelicans had consumed were packed with toxic diatoms (*Pseudo-nitzschia australis*). In Washington and Oregon, high levels of domoic acid were found in edible tissues of razor clams (*Siliqua patula* Dixon; Buck et al. 1992). With assistance in corroboration and counsel from Canadian scientists, as well as federal assistance from the U.S. National Marine Fisheries Service and the U.S. Food and Drug Administration, Pacific Coast states developed monitoring programs and shellfish harvesting closures to protect human health (Anonymous 1991, Fritz et al. 1992, Horner and Postel 1993). Officials closed the commercial and recreational fishery for nearly eight months, which translated into an ~U.S. $20 000 000 loss (U.S. Food and Drug Administration 1992, Horner and Postel 1993). An economically depressed area of the Northwest suffered the greatest hardship, including the consequence that consumers avoided all shellfish from the area, although commercially grown oysters (*Crassostrea gigas* Thun.) and mussels (*Mytilus edulis* L.) were tested as uncontaminated. During late fall

1991, domoic acid was also detected in the viscera of Dungeness crabs (*Cancer magister* Dana) from California to Washington (Horner and Postel 1993). This important commercial fishery also was closed for several weeks until proper cleaning of the crabs prior to cooking was determined adequate to prevent human exposure (Anonymous 1991, Washington Department of Health 1992). A retrospective epidemiology study by the Washington Department of Health reported 21 people from coastal communities in that state with gastrointestinal symptoms after they consumed razor clams in fall 1991; 13 of these individuals also sustained mild neurological symptoms (Quick 1992, Horner and Postel 1993).

Management approaches in confronting *Pseudonitzschia* spp. are presented in contrast to the case of *Pfiesteria*-like dinoflagellates. The representative species, *P. piscicida,* is the only species that has been formally named (Steidinger et al. 1996*a, b*), but at least four species, including *P. piscicida,* have been shown to be toxic to fish (Landsberg et al. 1995, Burkholder and Glasgow 1997). *P. piscicida* was identified in 1991 as a causative agent of major fish kills in the Albemarle-Pamlico estuarine system of North Carolina in the southeastern United States (Table 6; Burkholder et al. 1992). This system contributes approximately half of the surface area used as nursery grounds for fish species from Maine to Florida, and it is the second largest estuary on the U.S. mainland (Epperly and Ross 1986, Steel 1991). Since 1991, when they were first tracked to fish kills in the wild, at least three *Pfiesteria-like* species have been implicated as significant causative agents of major fish kills in the Albemarle-Pamlico and, more recently, the Chesapeake Bay (10^3–10^9 finfish and shellfish; Burkholder et al. 1995*a*, Burkholder and Glasgow 1997). In laboratory experiments, these dinoflagellates have been demonstrated to cause lesions in fish that become colonized by opportunistic bacteria and fungi (Noga et al. 1996, Burkholder and Glasgow 1997). This phenomenon is sometimes called ulcerative "mycosis" in the commercially important species, Atlantic menhaden (*Brevoortia tyrannus* Latrobe; North Carolina Division of Marine Fisheries [NC DMF] 1993), fish that form large, dense schools and are known for copious oily secretions that stimulate *P. piscicida* (Burkholder et al. 1992, 1995*a*). Atlantic menhaden have comprised ~90% of the affected fish in kills related to *Pfiesteria*-like dinoflagellates, although most other finfish and shellfish within a toxic outbreak area also die (Burkholder et al. 1995*a*). *P. piscicida* has been linked to immune system suppression, neurological impairment, and other sublethal/chronic health impacts in finfish (Table 4), and to shellfish diseases as well (e.g., shell disease in blue crab; H. B. Glasgow and J. M. Burkholder, *unpublished data*). A lipophilic toxin component from *P. piscicida* that causes epidermal sloughing in finfish has been isolated (D. Baden and U. Miami, *personal communication,* 1997). Toxins are contained in both water-soluble and lipophilic fractions (Burkholder 1997; J. M. Burkholder and laboratory group, with the National Institute of Environment Health Sciences Intramural Program and the National Marine Fisheries Service, Charleston, South Carolina, USA; *unpublished data* testing impacts to fish and mammalian tissues).

Despite the fact that *P. piscicida* was verified as a fish-killing agent by multiple laboratories (Noga et al. 1993, Lewitus et al. 1995*b*, Steidinger et al. 1995, 1996), with the research published in peer-reviewed international science journals, the researchers who brought the information to the attention of state authorities (the Division of Environmental Management, North Carolina Department of Environment, Health and Natural Resources [NC DEHNR]) were informed that 10 yr of data would be required before regulatory officials would be willing to consider the possibility that the organism might kill fish. For seven years, the agency refused to add information about toxic *Pfiesteria*-like dinoflagellates to state fish kill records or plankton datasets, so that these organisms officially did not exist (fish kill database, North Carolina Division of Water Quality, Raleigh, North Carolina, USA; Burtman 1995). This was done despite the fact that toxicity of field populations at fish kills was confirmed in experimental bioassays before implicating *Pfiesteria*-like species as causative agents (Burkholder et al. 1992, 1995, Burkholder and Glasgow 1997). Publications and reports about *Pfiesteria*'s role in fish kills, fish epizootics, and human health impacts were submitted to certain higher NC DEHNR personnel (e.g., Burkholder et al. 1992, 1993, Glasgow et al. 1995). But the officials disseminated misinformation about the researchers, claiming that the lead scientist had never published in refereed science journals (Barker 1977).

When 10 people were affected, 3 seriously, from exposure to toxic aerosols while working with dilute toxic cultures at field densities (equivalent to typical field population densities of *Pfiesteria* at fish kills) (Glasgow et al. 1995), state health officials attempted to disregard the information (Samolinski 1995, Barker 1997; videotaped television program "North Carolina Open Net," July 1997). This occurred despite state and federal mandates that further work with toxic cultures of *Pfiesteria*-like dinoflagellates required specially designed biohazard III facilities (records of the Department of Environmental Health Safety, North Carolina State University 1994), and despite a sizeable settlement of a worker's compensation case by the North Carolina Attorney General in favor of a severely affected laboratory worker (~U.S. $110 000, January 1994; Franklin 1995). The officials' lack of acknowledgment stemmed, in part, from the fact that the toxin(s) had not yet been fully characterized, so that concrete linkages with human health impacts in the field

could not be established. But the toxins have not been well characterized from many harmful algae that are known to cause serious human health effects (Falconer 1993*a*). State environmental health officials received a funding appropriation for use in *Pfiesteria* research, including controlling environmental influences and toxin identification, which was needed to characterize the organism's influence on fish and humans. Nearly two years passed, however, before a small portion of the funds was granted for research by the scientists whose proposal had been used initially to secure the appropriation through the governor (Barker 1997). Meanwhile, environmental health officials used the lack of information on toxin identity to state that there was no threat to tourists because clinics had never reported any confirmed *Pfiesteria*-related human cases, erroneously implying that physicians were able to test for it and rule it out (e.g., Music 1997).

Experiments and supporting field studies by the researchers strongly linked *Pfiesteria* to stimulation by nutrient enrichment, both directly and as an indirect effect mediated by algal prey (e.g., Burkholder et al. 1993, 1994, 1995*b*, Glásgow et al. 1995). NC DEHNR officials who were concerned about negative publicity, and who were pressured by certain industries such as seafood industry lobbyists, concentrated animal operations, and coastal developers (Barker 1997), worked with a local granting agency that heavily promotes the state's seafood and aquaculture industries to fund a study testing nutrient enrichment effects on *P. piscicida.* The scientists selected had no experience working with *P. piscicida* or other Pfiesteria-like dinoflagellates in any stage of their complex life cycles (Burkholder and Glasgow 1995, 1997, Steidinger et al. 1996), but the team leader publicly had stated strong disbelief in linkages between *Pfiesteria* and both fish kills and anthropogenic nutrient enrichment (Barker 1997). Several months later, the team leader made local news headlines when he reported strong linkages between *P. piscicida* and nitrogen enrichment (Rich 1996). After several more months, however, when involved in a news release from the granting agency to encourage tourism and calm negative press that linked *Pfiesteria* to water pollution, the team leader reported that the dinoflagellate he was studying is not stimulated by nutrient enrichment (North Carolina Sea Grant 1997).

Divers, docksmen, fishermen, and other local citizens began to report numerous symptoms (e.g., open sores that healed slowly and did not respond to antibiotics, burning skin or eyes, respiratory distress, short-term memory loss, disorientation, easy infections; Barker 1997) that were similar to those experienced by the laboratory workers (Glasgow et al. 1995). These symptoms have been sustained during North Carolina's "fish kill season," which has lasted for three months or more during most summers since 1987, usually involving death of $>10^6$ fish in numerous kills annually (Mather 1988, Burkholder et al. 1995*a*, Burkholder and Glasgow 1997). During a 6-wk period in 1995, when no other causative factors could be identified, 15×10^6 fish died with bleeding ulcerations ($\leq$4 cm in diameter; Burkholder et al. 1995*a*) while *P. piscicida* was swarming in the waters of the Neuse Estuary (Diaby 1996, Burkholder and Glasgow 1997). Higher NC DEHNR officials attempted to deny that the kill was related to *Pfiesteria,* but then learned that a widely circulated press interview by an agency field biologist had affirmed that the symptoms manifested by the fish were classical for this dinoflagellate (Associated Press 1995). Economically depressed people commonly were seen gathering dead fish with sores for consumption, but there were no steps taken by state officials to remove and discard accumulating dead fish, or to post warnings or advisements about handling/consuming fish that were dead and diseased when taken. Three weeks and 10×10^6 dead fish into the ongoing kill, local citizens demanded in public forums that the highest official in the state's environmental agency tour the fish kill area where *P. piscicida* toxic stages were active. When he saw fish dying with bleeding sores across a 35-km^2 area, experienced the stench of the rotting fish, and watched uninformed people gathering them for consumption, he prevailed on health officials within his agency to issue a warning against such practice (NC DEHNR 1995*b*).

National press about the issue led to refusal by some fish houses in other states to buy fish from any North Carolina waters (Diaby 1996). To protect the fisheries' economic health in other areas, state officials closed the 35-km^2 affected region of the Neuse Estuary to all fishing activity (NC DMF 1995). State health officials conducted a telephone survey, and then a limited written questionnaire, which were used to downplay the potential for human health effects from *Pfiesteria* (Morris 1996). People using the estuaries who developed epidermal lesions, burning eyes or skin, respiratory difficulties, disorientation, or other symptoms during in-progress, *Pfiesteria*-related fish kills were excluded from consideration if they had sustained sore throats or colds at any time for several weeks prior to the kills. Many who had been in fish kill areas avoided participation in the survey or in other interactions with state health officials, expressing distrust of the officials' motives (e.g., Brodeur 1995, Barker 1997). Some state environmental health officials also maintained that human health complaints from areas of toxic outbreaks by *Pfiesteria*-like dinoflagellates stemmed from naturally occurring bacteria, or from swimmer's itch caused by toxic blue-green algal species that are known in North Carolina to be mostly freshwater rather than estuarine (e.g., Paerl et al. 1984). These officials advised that it would be safe for small children in summer camps to swim in areas where toxic populations of *Pfiesteria* were related to in-progress ulceration epi-

zootics in fish, as long as they did not see dead fish. In counsel provided by a North Carolina environmental health official in an open letter to coastal citizens, rudimentary precautions (avoiding the area, not consuming fish that were dead when caught) were recommended only for areas where dead rather than diseased fish were obvious (Music 1997).

Working with the local aquaculture-focused granting agency, NC DEHNR also funded an epidemiology study led by an anthropologist. The study consisted of a questionnaire for crab fishermen. The public was informed that the study would determine whether *P. piscicida* affects human users of estuarine waters (press release by North Carolina Sea Grant, December 1995). But the researchers, who were unfamiliar with this organism or its effects, were instructed by state health officials that there were no reliable data about the biology or distribution of these dinoflagellates (Barker 1997). Several months after the study was funded, the anthropologist presented a seminar entitled, "Public Health and *Pfiesteria*: Preliminary Findings of a Research Report" but, remarkably, he did not mention *Pfiesteria* throughout his presentation. When queried by the audience, he admitted that he did not know how, or whether, data from his occupational study of crab fishermen could be related to the toxic dinoflagellates (North Carolina Sea Grant 1996). He did not have maps of toxic outbreaks by *Pfiesteria*-like dinoflagellates before he publicly interpreted his data. Many commercial fishermen admitted anonymously that they had avoided the survey despite having health problems that they perceived as water related, or had under-reported their symptoms because they feared potential negative impacts to their livelihoods or their industry (Barker 1997). Evidence that indicated severe learning and memory impairment for mammals in controlled experimental toxin exposures (Levin et al. 1997) was cursorily mentioned in a press release prior to the onset of the coastal tourism season, which used the anthropologist's statements to inform the public that watermen in the Neuse generally are healthy, and that there is no threat to human health from *Pfiesteria* in North Carolina's estuaries (North Carolina Sea Grant 1997). These results contrasted sharply with a petition to the U.S. Vice President, signed by ~140 coastal physicians, who requested assistance to alleviate water quality degradation resulting in increased incidence of epidermal lesions potentially related to *Pfiesteria*-like dinoflagellates and other waterborne diseases among their patients (Physicians of Craven County, North Carolina and surrounding areas 1997). In a related petition signed by 77 local physicians and presented to county officials, the presenting doctor stated, "Your doctors are telling you that those who use this river are getting sick, and the time to act is now" (Delaney 1997).

Seven years and $>1 \times 10^9$ dead fish with lesions after scientists' first formal reports to the regulatory agency about the role of *P. piscicida* and other *Pfiesteria*-like dinoflagellates in major fish kills, the stance of water quality officials in NC DEHNR and affiliated scientists was that estuarine fish kills are related to natural conditions that do not involve these dinoflagellates—for example, low dissolved oxygen—with *Pfiesteria*-like dinoflagellates at most, minor secondary stressors and opportunistic parasites that cannot, themselves, kill fish (NC DEHNR 1995*b*, 1997*a*, Paerl and Pinckney 1996), rather than toxic predators that repeatedly have been shown to kill healthy fish in minutes to hours (Burkholder et al. 1992, 1995*a*, Burkholder 1997). Reports on major fish kills linked to *Pfiesteria*-like dinoflagellates that occurred in areas where oxygen stress was not a preceding/present factor (Burkholder et al. 1995*a*, Burkholder and Glasgow 1997) were ignored. Even the 15×10^6 kill of fish with bleeding sores that was linked to *P. piscicida* during September and October 1995 (NC DEHNR report by Diaby 1996, Burkholder and Glasgow 1997) was attributed, two years later, to low dissolved oxygen (NC DEHNR 1997*b*), despite documentation that dissolved oxygen levels were well above 5 mg/L (state standard for fish health protection; NC DEHNR 1996) for several weeks prior to, and throughout, the kill. Official recognition of linkages between *Pfiesteria*-like dinoflagellates and fish disease also has been lacking (NC DEHNR 1995*a*, 1997*a*, *b*), despite the fact that ulceration epizootics (weeks to months in duration) coinciding with toxic populations of *Pfiesteria*-like species have affected ≤98% of all fish species and individuals in wide expanses of some North Carolina estuaries each year, at least since 1991 (Burkholder et al. 1995*a*, Burkholder and Glasgow 1997).

Furthermore, water-soluble lipophilic toxins from *P. piscicida* have been isolated and purified (Burkholder 1997; J. Ramsdell, P. Moeller, and colleagues, National Marine Fisheries Service, Charleston; F. Johnson and M. Snell, National Institute of Environment Health Sciences; and H. Glasgow, N. Deamer-Melia, and J. M. Burkholder, *unpublished data*). Upon exposure to water-soluble toxins associated with fish-killing *P. piscicida* cultures, fish have become moribund in 2–3 s, with death in 3–5 min (Burkholder 1997).

Environmental/health officials in states such as Maryland and Delaware learned from North Carolina's failures in addressing fish and human health issues related to *Pfiesteria*-like dinoflagellates (Shiffer 1997). In October 1996, reports of many fish with bleeding sores on the Pocomoke Estuary, Maryland, coincided with reports of fishermen with epidermal lesions, burning eyes and skin, disorientation/short-term memory loss, respiratory distress, and other symptoms (Maryland Department of Natural Resources, Maryland Department of Health and Mental Hygiene 1996). The problem persisted for several weeks in autumn, and recurred in April–May 1997. Despite negative pressure

from some seafood industry officials, fishermen publicly demanded that the water-related health symptoms that they and fish in the Pocomoke were experiencing be addressed. In August 1997, state officials convened a technical committee of scientists to provide guidance; a concerted sampling effort was deployed to characterize pollutant sources and potential fish pathogens including *Pfiesteria*-like dinoflagellates as well as other microbes; and a team of medical specialists from Johns Hopkins and the University of Maryland worked with state health officials, the National Institute of Environmental Health Sciences Intramural Program, and the Centers for Disease Control to design an epidemiology survey of watermen and recreationists who had frequented the Pocomoke during fish epizootics. When kills of 5×10^4 juvenile Atlantic menhaden in the Pocomoke, the Chicamacomico, and a Minoken River tributary were related to *P. piscicida* and a second *Pfiesteria*-like dinoflagellate—the same species known to occur in North Carolina estuaries—the affected areas as well as peripheral areas where fish were developing lesions were closed to fishing and most human contact until well after *Pfiesteria* specialists advised that the toxic outbreak had terminated. Within a 6-wk period, the medical specialists concluded that, among 22 people evaluated, 17 had symptoms that could not be explained by plausible causes other than toxic activity of *P. piscicida* and a second *Pfiesteria*-like species (identities confirmed by J. Burkholder and K. Steidinger, Florida Department of Environmental Protection, Florida Marine Research Institute). This effort provided the first strong link that was recognized by state and federal officials between fish kills/disease, *Pfiesteria*-like dinoflagellates, and human health problems in a field setting (Shields 1997*a*, *b*; L. M. Grattan et al., *unpublished manuscript*). A panel of scientists convened by the Governor of Maryland also reviewed all available data, and reached unanimous consensus that *P. piscicida* and other toxic *Pfiesteria*-like dinoflagellates can be stimulated by anthropogenic nutrient loading (Boesch 1997). Delaware state officials also sought guidance from *Pfiesteria* specialists following an open-lesion epizootic in finfish from the Indian River inland bay, and developed a proactive sampling program as well as literature for public education outreach on the issue.

These two case studies illustrate the reality that without local governments assuming responsibility and/or without federal involvement following the catastrophe of human death or obvious, serious human illness that can be fairly easily related, little progress historically has been realized in development of effective management strategies to mitigate sublethal chronic impacts to the health of humans, or fish, from harmful marine microalgae. Epidemiologists are convinced, nonetheless, that harmful microalgae-related human illnesses have significantly increased over the past decade, and that these diseases are significantly under-reported because the toxins can affect the immune system and their milder symptoms "mask" or mimic those of more well-known common diseases (e.g., CFP, PSP, DSP, ASP; Hokama and Miyahara 1986, Falconer 1993*a*, Hallegraeff 1993). For example, some ciguateratoxins are considered 100-fold more potent than brevetoxins (NSP). There is no available ciguateratoxin standard or official assay and, thus, no proactive testing program (Falconer 1993*a*). Yet, ciguatera comprises 33% of the known fishborne human illnesses worldwide (1977–1984), with ~100 fish species implicated as potential vectors for the toxin(s) (Hokama and Miyahara 1986). The noted increases in ciguatera from tropical regions over the past two decades have been attributed to coincidental factors such as a better informed public, increased travel to areas such as the West Indies and the South Pacific, extension of fishing grounds and shipping access, and ease of publishing cases (Hokama and Miyahara 1986). Another factor invoked for increased ciguatera is human and natural disturbance of coral reefs and island biota (Hokama and Miyahara 1986, Landsberg 1995). Increased sedimentation and sewage stimulate increased macroalgal cover that is potentially available for epiphytism by toxic ciguatera dinoflagellates, while live rock harvest (practice wherein thousands of tons of live coral reef have been legally jackhammered on a daily basis for removal and sale to aquarium entrepreneurs), herbivorous fish harvest, and other fishing-related disturbance lead to decreased herbivory on macroalgae. Some CFP dinoflagellate species are primary colonizers of opportunistic macroalgae after disturbance events (Anderson and Lobel 1987, Lewis and Ruff 1993, Landsberg 1995). In other regions, linkages are also beginning to be made between outbreaks of harmful heterotrophic dinoflagellates, anthropogenic nutrient loading, and impacts to both fisheries and human health (Glasgow et al. 1995, Burkholder and Glasgow 1997).

In confronting documented declines in wild stocks of many fish species throughout the world, management strategies increasingly have invoked aquaculture for sustaining supplies of fish resources (DeFur and Rader 1995, Safina 1995). By attempting to stimulate high-density growth of shellfish and finfish in contained systems, however, aquaculture presents an inadvertent bioassay for detecting harmful microalgae and heterotrophic dinoflagellates (Hallegraeff 1993). In areas where these organisms previously were undetected, the presence of abundant captive fish and their excreta has triggered outbreaks and led to heavy economic losses sustained by the aquaculturists (Shumway 1990, Hallegraeff 1993). As managers move toward encouraging aquaculture, additional outbreaks of harmful algae may be expected (Hallegraeff 1993, Sindermann 1996).

Recommendations for Sustainable Fisheries Management

Species of harmful marine microalgae and heterotrophic dinoflagellates that are apparently independent

of human influence represent a stochastic variable that will continue to confound our ability to accurately predict fish population size, physiological condition, and recruitment success. Despite the fact that some of these taxa have caused massive fish mortality for thousands of years, they do not exist in isolation from human activities that may, under certain circumstances, encourage their growth. For example, photosynthetic or mixotrophic species such as *Gymnodinium breve,* which develop blooms offshore (Steidinger and Baden 1984), could be stimulated by anthropogenic nutrient loadings in atmospheric deposition. They also could be stimulated by anthropogenic nutrient loadings, in inorganic or organic forms (Wilson 1968), when blooms are moved to nearshore areas. Warm-optimal taxa might be expected to increase in activity and expand or shift their geographic range if warming trends in global climate change continue (Epstein et al. 1994). Review of the available literature points to a critical need for a more proactive, concerted effort to "know the enemy." The gaps in our understanding of these organisms—whether apparently encouraged by human activities or not—and the extent of their impacts on marine fisheries loom large. In many cases, even information as basic as their identity and their life cycles remains to be researched (e.g., Estep and MacIntyre 1989, Burkholder and Glasgow 1995).

Accumulating evidence indicates that these harmful species significantly affect marine fisheries at the population level, well beyond the obvious acute impacts of fish kills. The scientific community has provided the direction (Anderson 1995) and must, in turn, be provided the means to obtain essential information about harmful microalgae and heterotrophic dinoflagellates that will enable managers to factor their adverse impacts into reliable models for sustainable fisheries management. Advanced technology is available to improve rapid, accurate detection of these harmful species through, for example, development of molecular probes and remote sensors where appropriate (Anderson 1995). A second critical need is for concerted efforts to identify toxins, and for rapid, reliable, economical methods to detect and quantify the toxins in water and aerosols, and in tissues of both wild and cultured fish. Such methods would strengthen sound guidance on food safety since it would facilitate testing of seafood and seafood products for the presence of these toxins (van Egmond et al. 1992, Falconer 1993*a*, Wright 1995). Improved methods for toxin detection and quantification would also help in marketing issues and in stemming economic impacts, by minimizing the uncertainty associated with consumption of fish from toxic outbreak areas (NC DMF 1995, Wright 1995, Burkholder and Glasgow 1997).

Improvement of management approaches in mitigating impacts from harmful marine microalgae and heterotrophic dinoflagellates on marine fisheries will also require strengthened insights about climatic influences, nutritional controls, and potential biocontrol feedbacks. Effective mechanisms are needed to move this information from research laboratories into regulatory agencies, where meaningful channels also must be developed to ensure that the information is seriously considered in developing improved strategies for mitigating fisheries impacts from harmful algal species. For scientific counsel to be formalized in a manner that will improve sustainable fisheries management, scientists who serve as formal or informal political appointees on advisory panels in environmental management agencies should be required to function within ethical constraints by being prohibited from receiving research funding that is influenced by the advisory panel, the agency, or political pressures that are brought to bear on these groups. The local agency that controls marine fisheries management should be formally meshed in decision-making processes with the agency that is charged to manage water quality and reduce habitat loss. Unfortunately, agencies and their advisory committees are often formed, instead, along conceptual but highly artificial boundaries of water quality vs. fisheries management, with the result that fisheries are cursorily or negligibly considered in permitting pollutant discharges, destruction of wetlands and submersed aquatic vegetation, and other decisions that influence habitat conditions in fish nursery and feeding grounds (Adler et al. 1993, Coastal Futures Committee 1994).

There is, additionally, a pressing and increasing need for development of surveillance and detection screening procedures to determine whether areas cited as favorable for aquaculture are conducive to growth of harmful microalgae and heterotrophic dinoflagellates. Screening for site suitability should involve careful analysis of both the water and sediments. Such proactive planning will reduce long-term economic loss to the aquaculture industry. Beyond these local considerations, management efforts related to harmful marine microalgae, and organized databases about the occurrence and effects of these species, need to be regionalized within the framework of coordinated networks on both national and international scales (e.g., Shumway 1990, Anderson 1995, Aune et al. 1996).

The issues of water quality and habitat degradation should be considered in developing strategies to mitigate effects on fish or their food supplies and habitat from harmful marine microalgae and heterotrophic dinoflagellates that have been linked to cultural eutrophication or other anthropogenic influences. For some of these species, correlations between abundance and nutrient loadings have been documented in limited experimental bioassays, but many of these organisms do not grow well under accepted mixing/suspension procedures for determining nutrient uptake kinetics (Dixon and Syrett 1988, Heil et al. 1993, Flynn and Flynn 1995). Some species also have shown poor response

to standard-sized microcosms and mesocosms in field and laboratory experimental approaches (Whitledge and Pulich 1991). Further difficulties in obtaining accurate insights have been confronted because some of these harmful microalgae have unusual nutritional limitations or complex requirements that involve both inorganic and organic forms of nitrogen, phosphorus, carbon, and other nutrients (Wilson 1968, Tomas and Baden 1993, DeYoe and Suttle 1994, Burkholder and Glasgow 1997). Research emphasis should be directed toward unraveling both direct and indirect trophic controls on these species. The underlying mechanisms for these controls, once known, will provide the necessary evidence and direction needed to improve water quality regulations to discourage growth of the harmful species through nutrient loading reductions, management of key predators, and other measures.

Increases in the frequency and spatial extent of blooms of harmful marine microalgae and heterotrophic dinoflagellates in both hemispheres (White 1988, Hallegraeff et al. 1990, Anderson 1995) suggest that these species have become an increasingly important component in determining year class strength of marine fishes through direct or indirect mechanisms (Robineau et al. 1991). As stated by Sindermann (1996), "These [coastal bloom] events raise the ante for [fish] individuals and species in terms of survival, by pushing harder on the adaptive strategies and responses that enable their continued existence in disturbed habitats." The impacts of harmful microalgae and heterotrophic dinoflagellates on marine fish populations merit serious consideration in developing management plans for sustainable fisheries. Without strengthened insights about these harmful species, we cannot hope to accurately predict aspects of such fundamental importance to wild or cultured fisheries as reproductive success, supply of beneficial food resources, ability to combat disease, and both short and long-term survival in the increasingly urbanized coastal setting.

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