

Red Tides

by Donald M. Anderson

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Many experts believe these blooms of toxic algae have recently become more prevalent, posing a greater threat to human and marine health

by Donald M. Anderson

Late in 1987 scientists faced a baffling series of marine catastrophes. First, 14 humpback whales died in Cape Cod Bay, Mass., during a five-week period. This die-off, equivalent to 50 years of "natural" mortality, was not a stranding, in which healthy whales beach themselves. Instead the cetaceans died at sea—some rapidly—and then washed ashore. Postmortem examinations showed that the whales had been well immediately before their deaths and that many of them had abundant blubber and fish in their stomachs, evidence of recent feeding. Alarmed and saddened, the public and press blamed pollution or a chemical spill for the mysterious deaths.

Two more mass poisonings occurred that month, but the victims in these new cases were humans. Fishermen and beachgoers along the North Carolina coast started complaining of respiratory problems and eye irritation. Within days, residents and visitors who had eaten local shellfish experienced diarrhea, dizziness and other symptoms suggesting neurotoxic poisoning. The illnesses bewildered epidemiologists and even prompted public conjecture that a nearby sunken submarine was leaking poison gas.

Concurrently, hospitals in Canada began admitting patients suffering from disorientation, vomiting, diarrhea and abdominal cramps. All had eaten

mussels from Prince Edward Island. Although Canadian authorities had dealt with shellfish poisoning outbreaks for decades, these symptoms were unfamiliar and disturbing: some patients exhibited permanent short-term memory loss. They could remember addresses but could not recall their most recent meal, for example. The officials quickly restricted the sale and distribution of mussels but eventually reported three deaths and 105 cases of acute poisoning in humans.

We now know that these seemingly unrelated events were all caused, either directly or indirectly, by toxic, single-celled algae called phytoplankton—vast blooms of which are commonly referred to as red tides. Although red tides have been recorded throughout history, the incidents mentioned above were entirely unexpected. As we shall see, they illustrate several major issues that have begun to challenge the scientific and regulatory communities.

Indeed, there is a conviction among many experts that the scale and complexity of this natural phenomenon are expanding. They note that the number of toxic blooms, the economic losses from them, the types of resources affected and the kinds of toxins and toxic species have all increased. Is this expansion real? Is it a global epidemic, as some claim? Is it related to human activities, such as rising coastal pollution? Or is it a result of increased scientific awareness and improved surveillance or analytical capabilities? To address these issues, we must understand the physiological, toxicological and ecological mechanisms underlying the growth and proliferation of red tide algae and the manner in which they cause harm.

Certain blooms of algae are termed red tides when the tiny pigmented plants grow in such abundance that they change the color of the seawater to red, brown or even green. The name is misleading, however, because many toxic events are called red tides even when the waters show no discoloration.

Likewise, an accumulation of nontoxic, harmless algae can change the color of ocean water. The picture is even more complicated: some phytoplankton neither discolor the water nor produce toxins but kill marine animals in other ways. Many diverse phenomena thus fall under the "red tide" rubric.

Of the thousands of living phytoplankton species that make up the base of the marine food web, only a few dozen are known to be toxic. Most are dinoflagellates, prymnesiophytes or chloromonads. A bloom develops when these single-celled algae photosynthesize and multiply, converting dissolved nutrients and sunlight into plant biomass. The dominant mode of reproduction is simple asexual fission—one cell grows larger, then divides into two cells, the two split into four, and so on. Barring a shortage of nutrients or light, or heavy grazing by tiny zooplankton that consume the algae, the population's size can increase rapidly. In some cases, a milliliter of seawater can contain tens or hundreds of thousands of algal cells. Spread over large areas, the phenomenon can be both visually spectacular and catastrophic.

Some species switch to sexual reproduction when nutrients are scarce. They form thick-walled, dormant cells, called cysts, that settle on the seafloor and can survive there for years. When favorable growth conditions return, cysts germinate and reinoculate the water with swimming cells that can then bloom. Although not all red tide species form cysts, many do, and this transformation explains important aspects of their ecology and biogeography. The timing and location of a bloom can depend on

RED TIDES appear when pigmented algae proliferate and form blooms. Even nontoxic species, including *Noctiluca*, shown blooming in a Japanese harbor, can kill marine animals by depleting the oxygen in shallow waters.

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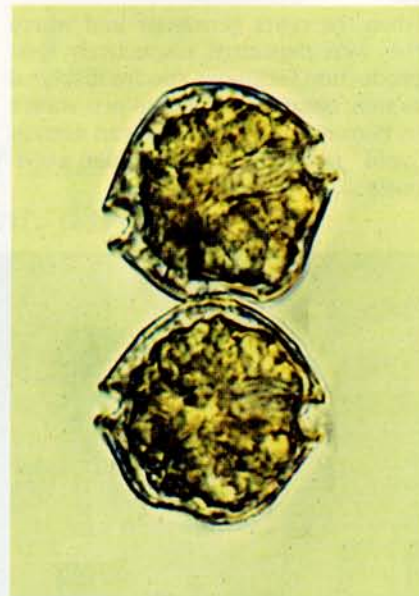
when the cysts germinate and where they were deposited, respectively. Cyst production facilitates species dispersal as well; blooms carried into new waters by currents or other means can deposit "seed" populations to colonize previously unaffected areas.

A dramatic example of natural dispersal occurred in 1972, when a massive red tide reaching from Maine to Massachusetts followed a September hurricane. The shellfish toxicity detected then for the first time has recurred in that region virtually every year now

for two decades. The cyst stage has provided a very effective strategy for the survival and dispersal of many other red tide species as well.

How do algal blooms cause harm? One of the most serious impacts on human life occurs when clams, mussels,





LIFE CYCLE of many toxic species enables them to survive for years under adverse conditions. When nutrients are scarce, the algae form thick-walled, dormant cysts (left). The cysts of-

ten travel into new waters. When favorable growth conditions return, the cysts germinate (center) and colonize previously unaffected areas with harmful organisms (right).

oysters or scallops ingest the algae as food and retain the toxins in their tissues. Typically the shellfish themselves are only marginally affected, but a single clam can sometimes accumulate enough toxin to kill a human being. These shellfish poisoning syndromes have been described as paralytic, diarrhetic and neurotoxic, shortened to PSP, DSP and NSP. The 1987 Canadian outbreak in which some patients suffered memory loss was appropriately characterized as amnesic shellfish poisoning, or ASP. The North Carolina episode was NSP.

A related problem, ciguatera fish poisoning, or CFP, causes more human illness than any other kind of toxicity originating in seafood. It occurs predominantly in tropical and subtropical islands, where from 10,000 to 50,000 individuals may be affected annually. Dinoflagellates that live attached to seaweeds produce the ciguatera toxins. Herbivorous fishes eat the seaweeds and the attached dinoflagellates as well. Because ciguatera toxin is soluble in fat, it is stored in the fishes' tissues and travels through the food web to carnivores. The most dangerous fish to eat are thus the largest and oldest, often considered the most desirable as well.

Symptoms do vary among the different syndromes but are generally neurological or gastrointestinal, or both. DSP causes diarrhea, nausea and vomiting, whereas PSP symptoms include tingling and numbness of the mouth, lips and fingers, accompanied by general muscular weakness. Acute doses inhibit respiration, and death results from respiratory paralysis. NSP triggers diarrhea,

vomiting and abdominal pain, followed by muscular aches, dizziness, anxiety, sweating and peripheral tingling. Ciguatera induces an intoxication syndrome nearly identical to NSP.

Illnesses and deaths from algal-derived shellfish poisons vary in number from year to year and from country to country. Environmental fluctuations profoundly influence the growth and accumulation of algae and thus their toxicity as well. Furthermore, countries differ in their ability to monitor shellfish and detect biotoxins before they reach the market. Developed countries typically operate monitoring programs that permit the timely closure of contaminated resources. Illnesses and deaths are thus rare, unless a new toxin appears (as in the ASP crisis in Canada) or an outbreak occurs in an area with no history of the problem (as in North Carolina). Developing countries, especially those having long coastlines or poor populations who rely primarily on the sea for food, are more likely to incur a higher incidence of sickness and death from algal blooms.

Phytoplankton can also kill marine animals directly. In the Gulf of Mexico, the dinoflagellate *Gymnodinium breve* frequently causes devastating fish kills. As the wild fish swim through *G. breve* blooms, the fragile algae rupture, releasing neurotoxins onto the gills of the fish. Within a short time, the animals asphyxiate. Tons of dead fish sometimes cover the beaches along Florida's Gulf Coast, causing several millions of dollars to be lost in tourism

and other recreation-based businesses.

Farmed fish are especially vulnerable because the caged animals cannot avoid the blooms. Each year, farmed salmon, yellowtail and other economically important species fall victim to a variety of algal species. Blooms can wipe out entire fish farms within hours, killing fingerlings and large fish alike. Algal blooms thus pose a large threat to fish farms and their insurance providers. In Norway an extensive program is under way to minimize these impacts. Fish farmers make weekly observations of algal concentrations and water clarity. Other parameters are transmitted to shore from instruments on moored buoys. The Norwegian Ministry of Environment then combines this information with a five-day weather forecast to generate an "algal forecast" for fish farmers and authorities. Fish cages in peril are then towed to clear water.

Unfortunately, not much more can be done. The ways in which algae kill fish are poorly understood. Some phytoplankton species produce polyunsaturated fatty acids and galactolipids that destroy blood cells. Such an effect would explain the ruptured gills, hypoxia and edema in dying fish. Other algal species produce these hemolytic compounds and neurotoxins as well. The combination can significantly reduce a fish's heart rate, resulting in reduced blood flow and a deadly decrease in oxygen.

Moreover, nontoxic phytoplankton can kill fish. The diatom genus *Chaetoceros* has been linked to dying salmon in the Puget Sound area of Washington State, yet no toxin has ever been identi-

fied in this group. Instead species such as *C. convolutus* sport long, barbed spines that lodge between gill tissues and trigger the release of massive amounts of mucus. Continuous irritation exhausts the supply of mucus and mucous cells, causing lamellar degeneration and death from reduced oxygen exchange. These barbed spines probably did not evolve specifically to kill fish, since only caged fish succumb to the blooms. The problems faced by fish farmers are more likely the unfortunate result of an evolutionary strategy by certain *Chaetoceros* species to avoid predation or to stay afloat.

Algal toxins also cause mortalities as they move through the marine food web. Some years ago tons of herring died in the Bay of Fundy after consuming small planktonic snails that had eaten the PSP-producing dinoflagellate *Alexandrium*. From the human health standpoint, it is fortunate that herring, cod, salmon and other commercial fish are sensitive to these toxins and, unlike shellfish, die before toxins reach dangerous levels in their flesh. Some toxin, however, accumulates in the liver and other organs of certain fish, and so animals such as other fish, marine mammals and birds that consume whole fish, including the viscera, are at risk.

We now can reconstruct the events that killed the whales in 1987. A few weeks of intense investigations that year by marine pathologist Joseph R. Geraci of the Ontario Veterinary College, myself and many others revealed that the PSP toxins most likely caused these deaths. The dinoflagellate *Alexandrium tamarense* produced the toxins, which reached the whales via their food web. We analyzed mackerel that the whales had been eating and found saxitoxin, not in their flesh but concentrated in the liver and kidney. Presumably the mackerel ate zooplankton and small fish that had previously dined on *Alexandrium*.

The humpbacks were starting their southward migration and were feeding heavily. Assuming that they consumed 4 percent of their body weight daily, we calculated that they received a saxitoxin dosage of 3.2 micrograms per kilogram of body weight. But was this a fatal dose? Unfortunately, in 1987 we had no data that directly addressed how much toxin would kill a whale. We knew the minimum lethal dose of saxitoxin for humans is seven to 16 micrograms per kilogram of body weight, but that was two to five times more than what the whales had probably ingested.

Our calculations were initially disheartening, but as we thought about it we realized that whales might be more

sensitive to the toxins than are humans. First, whales would have received continual doses of toxin as they fed, whereas human mortality statistics are based on single feedings. Second, during a dive, the mammalian diving reflex channels blood and oxygen predominantly to the heart and brain. The same mechanism sometimes protects young children who fall through thin ice and survive drowning, despite being underwater for half an hour or longer. For humans, cold water induces the reflex, but for whales, it is activated during every dive.

Each dive then would expose the most sensitive organs to the toxin, which would bypass the liver and kidney, where it could be metabolized and excreted. Finally, saxitoxin need not have killed the whales directly. Even a slightly incapacitated animal might have difficulty orienting to the water surface or breathing correctly. The whales may actually have drowned following a sublethal exposure to saxitoxin. The exact cause will never be known, but the evidence strongly suggests that these magnificent creatures died from a natural toxin originating in microscopic algae.

Other examples of toxins traveling up the food web appear nearly every year. In 1991 sick or dying brown pelicans and cormorants were found near Monterey Bay, Calif. Wildlife experts could

find no signs that pesticides, heavy metals or other pollutants were involved. The veterinarian in charge of the study telephoned Jeffrey Wright of the National Research Council laboratory in Halifax, Nova Scotia. Wright had directed the Canadian Mussel Toxin Crisis Team that identified the poison responsible for the mysterious ASP episode in 1987. His team had isolated a toxin from the Prince Edward Island mussels, called domoic acid, and traced it to its source—a diatom, *Pseudonitzschia pungens*, that had been considered harmless. Four years later members of the same Canadian team quickly ascertained that the sick and dying birds in California had eaten anchovies that contained domoic acid, again from *Pseudonitzschia* (but a different species).

The toxins responsible for these syndromes are not single chemical entities but are families of compounds having similar chemical structures and effects. For example, the saxitoxins that cause PSP are a family of at least 18 different compounds with widely differing potencies. Most algal toxins cause human illness by disrupting electrical conduction, uncoupling communication between nerve and muscle, and impeding critical physiological processes. To do so, they bind to specific membrane receptors, leading to

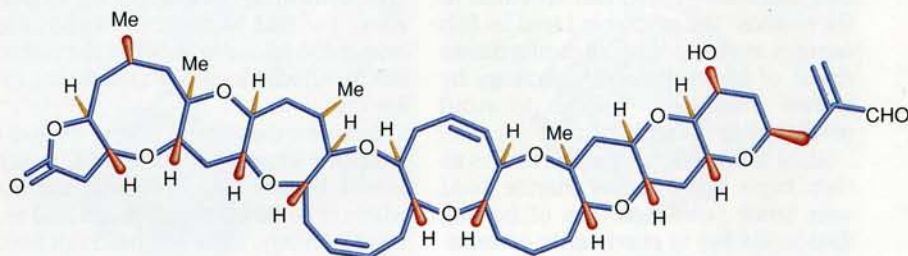


HUMPBACK WHALES, a total of 14, died suddenly from exposure to a bloom of *Alexandrium tamarense* in Cape Cod Bay, Mass., in 1987. Researchers later learned that the whales had eaten mackerel whose organs contained high concentrations of saxitoxin, a neurotoxin produced by the algae.

Algal Toxins

The structure of red tide toxins varies considerably. Saxitoxin compounds (one example shown at left) sport different combinations of H^+ , OH^- and SO_3^- on the R1 to R4 sites, but all members of this family block the sodium channel and thus prevent communication between neurons and muscles. H. Robert Guy of the National Institutes of Health has pro-

posed a structural model of this interaction (right). The carbon backbone of the sodium channel is colored gray, the carboxyls are red, nitrogen is blue, and hydrogen is white. Saxitoxin binds in the narrowest region of this channel. The brevetoxins (one example shown at center) that cause NSP are much larger molecules that also affect the sodium channel.



changes in the intracellular concentration of ions such as sodium or calcium.

The saxitoxins bind to sodium channels and block the flux of sodium in and out of nerve and muscle cells. Brevetoxins, the family of nine compounds responsible for NSP, bind to a different site on the sodium channel but cause the opposite effect from saxitoxin. Domoic acid disrupts normal neurochemical transmission in the brain. It binds to kainate receptors in the central nervous system, causing a sustained depolarization of the neurons and eventually cell degeneration and death. Memory loss in ASP victims apparently results from lesions in the hippocampus, where kainate receptors abound.

Why do algal species produce toxins? Some argue that toxins evolved as a defense mechanism against zooplankton and other grazers. Indeed, some zooplankton can become slowly incapacitated while feeding, as though they are being gradually paralyzed or otherwise impaired. (In one study, a tintinnid ciliate could swim only backward, away from its intended prey, after exposure to toxic dinoflagellates.) Sometimes grazing animals spit out the toxic algae as though they had an unpleasant taste. These responses would all reduce grazing and thus facilitate bloom formation.

All the same, nontoxic phytoplankton also form blooms, and so it is unlikely that toxins serve solely as self-defense. Scientists are looking within the algae for biochemical pathways that require the toxins, but the search thus far has been fruitless. The toxins are not proteins, and all are synthesized in a series of chemical steps requiring multiple genes. Investigators have proposed biosynthetic pathways, but they have not isolated chemical intermediates or en-

zymes used only in toxin production. It has thus been difficult to apply the powerful tools of molecular biology to these organisms, other than to study their genes or to develop detection tools.

We do have some tantalizing clues about toxin metabolism. For example, certain dinoflagellate strains produce different amounts of toxin and different sets of toxin derivatives when we vary their growth conditions. Metabolism of the toxins is a dynamic process, but we still do not know whether they have a specific biochemical role. As with the spiny diatoms that kill fish, the illnesses and mortalities caused by algal "toxins" may be the result of the accidental chemical affinity of those metabolites for receptor sites on ion channels in higher animals.

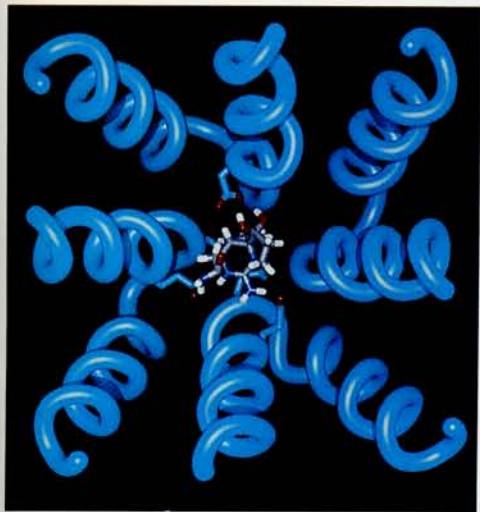
The potential role of bacteria or bacterial genes in phytoplankton toxin production is an area of active research. We wonder how a genetically diverse array of organisms, including phytoplankton, seaweeds, bacteria and cyanobacteria, could all have evolved the genes needed to produce saxitoxin [see "The Toxins of Cyanobacteria," by Wayne W. Carmichael; *SCIENTIFIC AMERICAN*, January]. Several years ago Masaaki Kodama of Kitasato University in Japan isolated intracellular bacteria from antibiotic-treated *A. tamarensis* cultures and showed that the bacteria produced saxitoxin. This finding supported an old and long-ignored hypothesis that toxins might originate from bacteria living inside or on the dinoflagellate cell.

Despite considerable study, the jury is still out. Many scientists now accept that some bacteria produce saxitoxins, but they point out that dense bacterial cultures produce extremely small quantities. It is also not clear that those bac-

teria can be found inside dinoflagellates. That intracellular bacteria produce all of the toxin found in a dinoflagellate cell therefore seems unlikely, but perhaps some synergism occurs between a small number of symbionts and the host dinoflagellate that is lost when the bacteria are isolated in culture. Alternatively, a bacterial gene or plasmid might be involved.

Given the diverse array of algae that produce toxins or cause problems in a variety of oceanographic systems, attempts to generalize the dynamics of harmful algal blooms are doomed to fail. Many harmful species, however, share some mechanisms. Red tides often occur when heating or freshwater runoff creates a stratified surface layer above colder, nutrient-rich waters. Fast-growing algae quickly strip away nutrients in the upper layer, leaving nitrogen and phosphorus only below the interface of the layers, called the pycnocline. Nonmotile phytoplankton cannot easily get to this layer, whereas motile algae, including dinoflagellates, can thrive. Many swim at speeds in excess of 10 meters per day, and some undergo daily vertical migration: they reside in surface waters by day to harvest sunlight like sunbathers, then swim down to the pycnocline to take up nutrients at night. As a result, blooms can suddenly appear in surface waters that are devoid of nutrients and would seem incapable of supporting such prolific growth.

A similar sleight-of-hand can occur horizontally, though over much larger distances. The NSP outbreak in North Carolina illustrates how ocean currents can transport major toxic species from one area to another. Patricia A. Tester,



a biologist at the National Oceanic and Atmospheric Administration's National Marine Fisheries Service laboratory in Beaufort, examined plankton from local waters under a microscope soon after the initial reports of human illnesses. She saw cells resembling the dinoflagellate *G. breve*, the cause of recurrent NSP along Florida's western coast. Experts quickly confirmed her tentative identification, and for the first time in state history, authorities closed shellfish beds because of algal toxins, resulting in a loss of \$20 million.

Tester and her co-workers have since used satellite images of sea-surface temperatures to argue that the *G. breve* population in North Carolina originated off the southwestern coast of Florida, nearly 1,000 kilometers away. That bloom traveled from the Gulf of Mexico up the southeastern coast of the U.S., transported by several current systems culminating in the Gulf Stream. After 30 days of transport, a filament of water separated from the Gulf Stream and moved onto North Carolina's narrow continental shelf, carrying *G. breve* cells with it. The warm water mass remained in nearshore waters, identifiable in satellite images for three weeks. Fortunately, *G. breve* does not have a known cyst stage, so it could not establish a seedbed and colonize this new region.

This incident, taken together with

WARM WATER PLUME (green), revealed in a satellite infrared image of sea-surface temperature, traveled from southern Maine into Massachusetts Bay in 1987, carrying *A. tamarense*. Remote-sensing techniques help investigators track blooms traveling within discrete water masses.

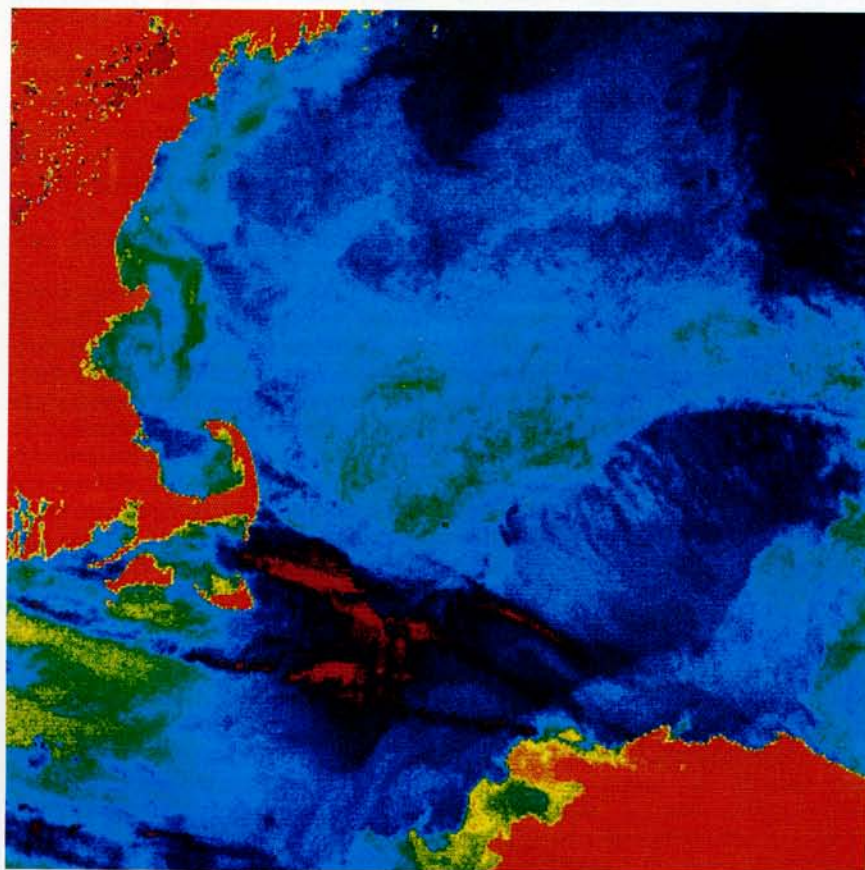
many others like it throughout the world, speaks of an unsettling trend. Problems from harmful red tides have grown worse over the past two decades. The causes, however, are multiple, and only some relate to pollution or other human activities. For example, the global expansion in aquaculture means that more areas are monitored closely, and more fisheries' products that can be killed or take up toxins are in the water. Likewise, our discovery of toxins in algal species formerly considered nontoxic reflects the maturation of this field of science, now profiting from more investigators, better analytical techniques and chemical instrumentation, and more efficient communication among workers.

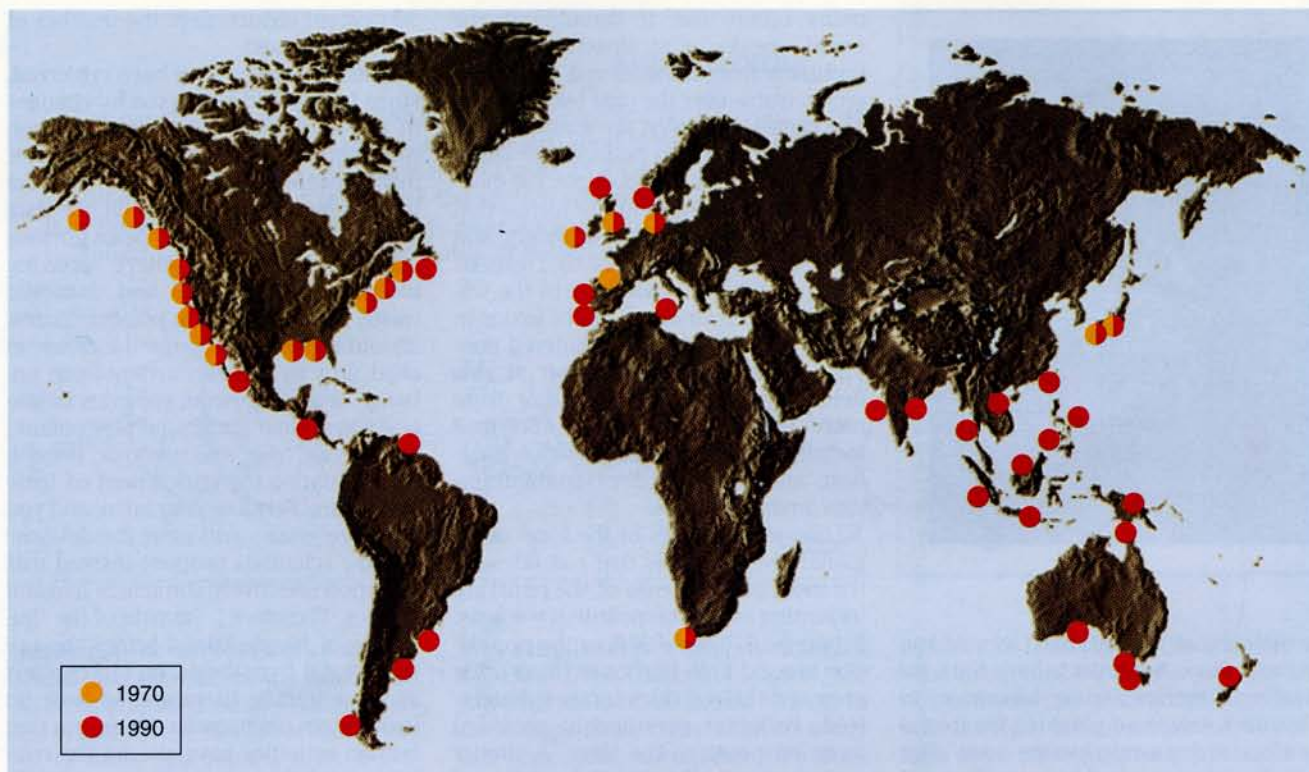
Long-term studies at the local or regional level do show that red tides (in the most general sense of the term) are increasing as coastal pollution worsens. Between 1976 and 1986, as the population around Tolo Harbor in Hong Kong grew sixfold, red tides increased eightfold. Pollution presumably provided more nutrients to the algae. A similar pattern emerged in the Inland Sea of Japan, where visible red tides proliferated steadily from 44 per year in 1965 to more than 300 a decade later. Japanese authorities instituted rigorous effluent controls in the mid-1970s, and a

50 percent reduction in the number of red tides ensued.

These examples have been criticized, since both could be biased by changes in the numbers of observers through time, and both are tabulations of water discolorations from blooms, not just toxic or harmful episodes. Still, the data demonstrate what should be an obvious relationship: coastal waters receiving industrial, agricultural and domestic waste, frequently rich in plant nutrients, should experience a general increase in algal growth. These nutrients can enhance toxic or harmful episodes in several ways. Most simply, all phytoplankton species, toxic and nontoxic, benefit, but we notice the enrichment of toxic ones more. Fertilize your lawn, and you get more grass—and more dandelions.

Some scientists propose instead that pollution selectively stimulates harmful species. Theodore J. Smayda of the University of Rhode Island brings the nutrient ratio hypothesis, an old concept in the scientific literature, to bear on toxic bloom phenomena. He argues that human activities have altered the relative availability of specific nutrients in coastal waters in ways that favor toxic forms. For example, diatoms, most of which are harmless, require silicon in their cell walls, whereas other phytoplankton do not. Because silicon is not





OUTBREAKS of paralytic shellfish poisoning affected more than twice as many areas in 1990 as they did in 1970. Some experts believe coastal pollution and shipping practices have contributed to the expansion.

abundant in sewage, but nitrogen and phosphorus are, the ratio of nitrogen to silicon or of phosphorus to silicon in coastal waters has increased over the past several decades. Diatom growth ceases when silicon supplies are depleted, but other phytoplankton classes, which often include more toxic species, can proliferate using "excess" nitrogen and phosphorus. This idea is controversial but not unfounded. A 23-year time series from the German coast documents a fourfold rise in the nitrogen-silicon and phosphorus-silicon ratios, accompanied by a striking change in the composition of the phytoplankton community: diatoms decreased, whereas flagellates increased more than 10-fold.

Another concern is the long-distance transport of algal species in cargo vessels. We have long recognized that ships carry marine organisms in their ballast water, but evidence is emerging that toxic algae have also been hitchhiking across the oceans. Gustaaf M. Hallegraeff of the University of Tasmania has frequently donned a miner's helmet and ventured into the bowels of massive cargo ships to sample sediments accumulated in ballast tanks. He found more than 300 million toxic dinoflagellate cysts in one vessel alone. Hallegraeff argues that one PSP-producing dinoflagellate species first appeared in Tasmanian waters during the past two

decades, concurrent with the development of a local wood-chip industry. Empty vessels that begin a journey in a foreign harbor pump water and sediment into their tanks for ballast; when wood chips are loaded in Tasmania, the tanks are discharged. Cysts easily survive the transit cruise and colonize the new site. Australia has now issued strict guidelines for discharging ballast water in the country's ports. Unfortunately, most other nations do not have such restrictions.

The past decade may be remembered as the time that humankind's effect on the global environment caught the public eye in a powerful and ominous fashion. For some, signs of our neglect come with forecasts of global warming, deforestation or decreases in biodiversity. For me and my colleagues, this interval brought a bewildering expansion in the complexity and scale of the red tide phenomenon. The signs are clear that pollution has enhanced the abundance of algae, including harmful and toxic forms. This effect is obvious in Hong Kong and the Inland Sea of Japan and is perhaps real but less evident in regions where coastal pollution is more gradual and unobtrusive. But we cannot blame all new outbreaks and new problems on pollution. There are many other factors that contribute to the proliferation of toxic species; some in-

volve human activities, and some do not. Nevertheless, we may well be witnessing a sign that should not be ignored. As a growing world population demands more and more of fisheries' resources, we must respect our coastal waters and minimize those activities that stimulate the spectacular and destructive outbreaks called red tides.

FURTHER READING

- PRIMARY PRODUCTION AND THE GLOBAL EPIDEMIC OF PHYTOPLANKTON BLOOMS IN THE SEA: A LINKAGE? Theodore J. Smayda in *Novel Phytoplankton Blooms: Causes and Impacts of Recurrent Brown Tide and Other Unusual Blooms*. Edited by E. M. Cosper, V. M. Bricelj and E. J. Carpenter. Springer-Verlag, 1989.
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- DOMOIC ACID AND AMNESIC SHELLFISH POISONING: A REVIEW. Ewen C. D. Todd in *Journal of Food Protection*, Vol. 56, No. 1, pages 69-83; January 1993.
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