

PERSPECTIVE

The role of microorganisms in coral bleaching

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Coral bleaching is the disruption of the symbiosis between the coral host and its endosymbiotic algae. The prevalence and severity of the disease have been correlated with high seawater temperature. During the last decade, the major hypothesis to explain coral bleaching is that high water temperatures cause irreversible damage to the symbiotic algae resulting in loss of pigment and/or algae from the holobiont. Here, we discuss the evidence for an alternative but not mutually exclusive concept, the microbial hypothesis of coral bleaching.

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Introduction

Coral reefs develop through the massive and long-term build-up of calcareous skeleta of scleractinian corals. These corals are modular cnidarians that secrete a CaCO₃ exoskeleton on and in which other organisms may grow. Scleractinian corals are made up of one or more polyps composed of an external protective body layer (ectoderm), an inner gastrodermal layer that carries out most of the coral's digestive and reproductive functions and between them an acellular mesoglea (Figure 1). The ectodermal layer that is apposed to the substrata produces CaCO₃ as a support for the coral tissue layers. In colonial forms, there is a tissue and gastrovascular confluence between polyps so that nutrients and signaling can be transferred between different parts of the colony. Corals are conduits to numerous microorganisms, including the intracellular zooxanthellae, other protists such as thraustochytrids, prokaryotes (bacteria and archaea) and viruses (Rohwer *et al.*, 2002; Wegley *et al.*, 2004; Kramarsky-

Winter *et al.*, 2006; Davy and Patten, 2007; Rosenberg *et al.*, 2007; Harel *et al.*, 2008; Marhaver *et al.*, 2008). Many of these organisms may be considered symbionts and play an important role in coral health.

Bleaching is defined as the disruption of the symbiosis between the coral host and its endosymbiotic zooxanthellae (of the genus *Symbiodinium*). This can be the result of the loss of the algal symbiont and/or of the algal pigments. The coral tissues then become transparent making the underlying white calcium carbonate skeleton visible. Other signs of bleaching include thinning of host tissue, reduction in mucus and often inhibition of sexual reproduction. If bleaching is not reversed, corals will die.

Various studies carried out during the last few years have led to the view that coral bleaching is a disease that is affected by biotic and environmental factors. A disease is defined as a process resulting in tissue damage or alteration of physiological function, producing visible symptoms (Stedman, 2005). Accordingly, coral bleaching is clearly a disease and should be referred to as such. Bleaching has been shown to be induced by a variety of factors, including high temperature and irradiance (reviewed in Jokiel, 2004), low salinity (Goreau, 1964), sediments (Peters, 1984), exposure to cyanide

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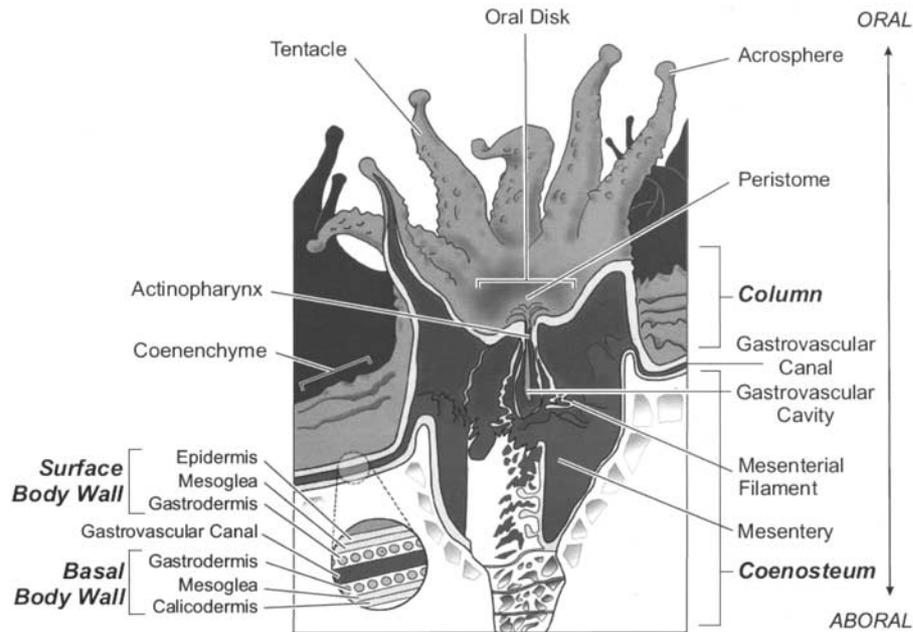


Figure 1 Anatomy of a polyp of a scleractinian coral (after Galloway *et al.*, 2007).

(Cervino *et al.*, 2003), decreased seawater temperature (Muscatine *et al.*, 1991) and bacterial infection (Kushmaro *et al.*, 1996, 1997; Ben-Haim and Rosenberg, 2002). All of these stressors caused bleaching both in the laboratory and in the sea (Brown, 1997).

During the last two decades, there have been reports of bleaching being caused by a variety of microbial pathogens. The assertion that these biotic agents were indeed the causative agent of this disease was demonstrated by applying Koch's postulates. Unfortunately, despite the growing evidence for the role of bacteria in coral bleaching and other diseases, there are still some authors who discount the direct effect that microorganisms play in the disease processes (for example, Ainsworth *et al.*, 2008).

The discovery of bacterial bleaching of corals

Extensive bleaching of the coral *Oculina patagonica* in the eastern Mediterranean Sea occurs every summer (Kushmaro *et al.*, 1996). Kushmaro *et al.* (1996, 1997) reported that the bleaching of *O. patagonica* was the result of an infection by *Vibrio shiloi* (Figure 2). The demonstration that *V. shiloi* was the causative agent of the disease was established by rigorously satisfying all of Koch's postulates, including the fact that bleached coral in the sea contained the bacterium (Kushmaro *et al.*, 1996, 1997), whereas it was absent from healthy corals (see Figure 3a). Furthermore, Kushmaro *et al.* (1998) showed that the infection and subsequent bleaching occurred only at temperatures above 25 °C. Thus, for bleaching to occur, both elevated

temperature and the causative agent must be present.

Steps in the infections of *O. patagonica* by *V. shiloi*

The specific steps in the infection of *O. patagonica* by *V. shiloi* have been studied extensively (Rosenberg and Falkovitz, 2004). The bacteria are chemotactic to the coral mucus, adhere to a β -galactoside-containing receptor on the coral surface, penetrate into the epidermal layer (Figure 3) and multiply intracellularly, reaching 10^8 – 10^9 cells per cm^3 . The intracellular *V. shiloi* produces an extracellular peptide toxin (PYPVYPPVVP) that inhibits algal photosynthesis. Another important factor for the virulence of *V. shiloi* is the expression of superoxide dismutase. Adhesion, production of the toxin and expression of superoxide dismutase are all temperature-dependent reactions, occurring at summer (25–30 °C) but not at winter (16–20 °C) temperatures. Thus, *V. shiloi* cannot infect, multiply or survive in the coral during the winter. Sussman *et al.* (2003) demonstrated that the marine fireworm *Hermodice carunculata* is a winter reservoir and spring–summer vector for *V. shiloi*.

Effect of ultraviolet radiation on bleaching of *O. patagonica*

One of the stress factors reported to induce bleaching on coral reefs is high solar radiation (Lesser *et al.*, 1990). Gleason and Wellington (1993) concluded that it was the high ultraviolet radiation that

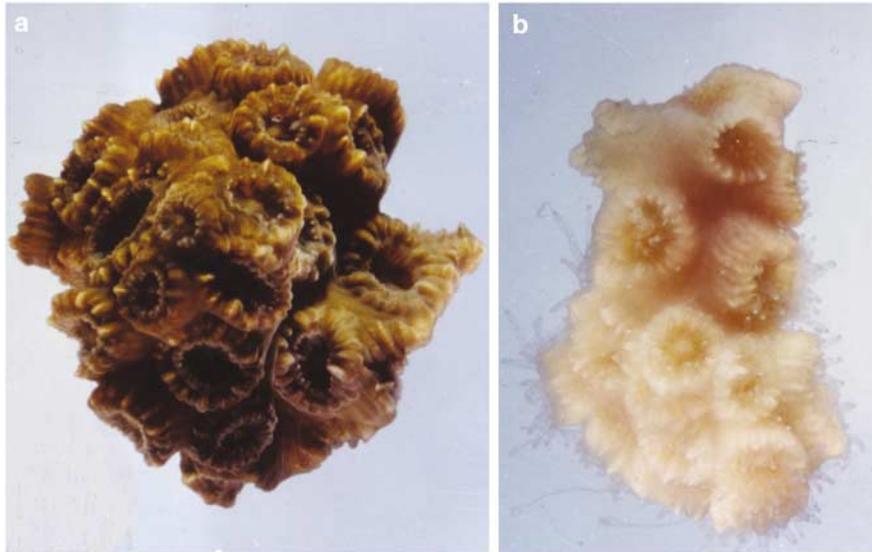


Figure 2 Photograph of bleached and unbleached colonies of *Oculina patagonica* collected from the Mediterranean coast of Israel.

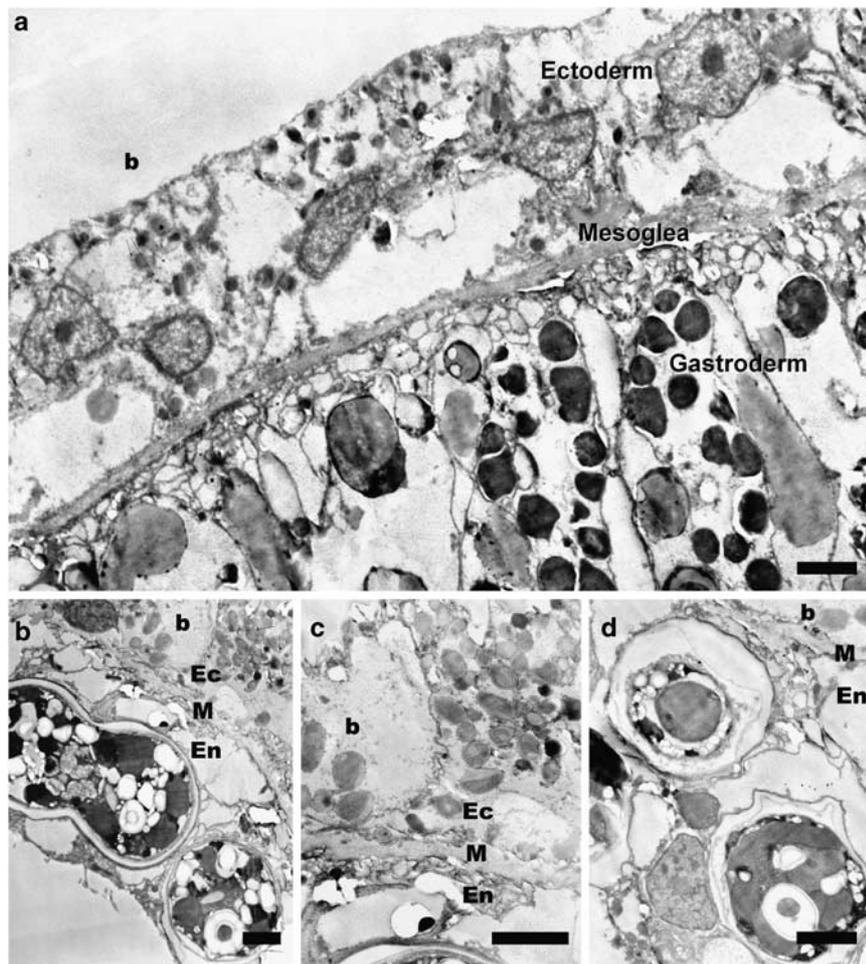


Figure 3 Transmission electron micrographs of the coral *Oculina patagonica* from 1996. (a) Naturally bleached colony collected on 29 July 1996 from Sdot Yam, Mediterranean coast, Israel at a water temperature of 29 °C. (b–d) Colony 18 h after experimental infection with *Vibrio shiloi* 10⁶ cells incubated at 29 °C in the lab. (b) Ectoderm with visible bacteria (b) and gastrodermis showing vacuolization in tissue surrounding zooxanthellae. (c) Enlargement of (b) showing the *Vibrio shiloi* in ectoderm adjacent to the necrotic tissue. (d) Breakdown of the zooxanthellae in the infected coral and their digestion by the host.

affected the corals inducing bleaching in *Montastrea annularis*. The generality of this conclusion was challenged when it was shown that colonies of *O. patagonica* in shallow water (0–80 cm) tidal pools (high ultraviolet radiation) showed negligible bleaching, even though summer temperatures there in shallow water were 2–4 °C warmer than in the open water (Fine *et al.*, 2002). In this study, fragments transplanted from 4 m depth to shallow reef flats (>30 cm depth) in May showed no bleaching, whereas fragments transplanted from the shallow reef to 4 m depth underwent extensive bleaching. Moreover, when *O. patagonica* was incubated with *V. shiloi* in aquaria exposed to bright sunlight, the bacteria were rapidly killed and no bleaching occurred. However, when the corals were protected from ultraviolet light with a Pexiglass filter, *V. shiloi* multiplied and bleaching was induced. Thus in the case of bacterial bleaching of *O. patagonica*, ultraviolet radiation actually inhibits bleaching occurring in very shallow water (<80 cm depth) by killing the pathogen (Fine *et al.*, 2002).

Bacterial bleaching of *Pocillopora damicornis* by *Vibrio coralliilyticus*

The coral *O. patagonica* is a temperate Mediterranean coral not found on coral reefs, so it was important to test whether bacterial pathogens could also cause bleaching of reef corals. A new species *Vibrio coralliilyticus* was initially isolated from a bleached coral, *Pocillopora damicornis*, present on the Zanzibar coral reef (Ben-Haim and Rosenberg, 2002; Ben-Haim *et al.*, 2003). When bleaching of *P. damicornis* was observed on the Eilat coral reef, *V. coralliilyticus* was isolated from five different bleached coral colonies. It was absent from healthy corals. Using the different *V. coralliilyticus* strains, it was demonstrated that this *Vibrio* species is an etiological agent, bleaching *P. damicornis* in the Indian Ocean and Red Sea.

The infection of *P. damicornis* by *V. coralliilyticus* shows strong temperature dependence (Ben-Haim *et al.*, 2003). Below 22 °C no signs of infection occurred. From 24 to 26 °C, the infection resulted in bleaching, whereas from 27 to 29 °C the infection caused rapid tissue lysis. Earlier, Jokiel and Coles (1990) reported that corals undergo tissue lysis following bleaching when the temperature is elevated. In the case of *V. coralliilyticus* infection, the tissue lysis was shown to be the result of the synthesis of a potent metalloproteinase by the pathogen at temperatures above 26 °C.

Association of *Vibrio* spp. with bleached corals in the Caribbean and Great Barrier Reef

Ritchie *et al.* (1994) enumerated the culturable heterotrophic bacteria of bleached and healthy

Montastrea annularis coral colonies in the Caribbean. *Vibrio* spp. were never isolated from healthy corals but represented 30% of isolates from bleached corals. A similar shift in the bacterial community occurred on *Agaricia* sp. during the 1995–1996 and 1998–1999 bleaching events on reefs of San Salvador Island, Bahamas (McGrath and Smith, 1999). Prior to bleaching, *Vibrio* comprised ca. 20%, whereas during bleaching they rose to 40% and at the height of bleaching they represented over 60% of the culturable bacteria. When the corals recovered, the *Vibrio* population decreased to 20%. Clearly, these pioneering experiments could not distinguish between the *Vibrio* being the cause or result of the disease.

Bourne *et al.* (2008) carried out a comprehensive study of changes in the microbial composition of the coral *Acropora millepora* over 2.5 years, which included a severe bleaching event on the Great Barrier Reef (January–February 2002). The data obtained by culture-independent techniques led to several important conclusions: (i) as corals bleached, the microbial community shifted, revealing a correlation between increasing temperature and the appearance of *Vibrio*-affiliated sequences; (ii) this shift commenced prior to visual signs of bleaching and (iii) the coral microbial associations shifted again after the bleaching event, returning to a profile similar to the fingerprints obtained prior to bleaching. The authors suggest that microbial shifts can act as an indicator of stress prior to the appearance of visual signs of bleaching. They speculate further that the temperature-induced change in the microbial community prior to bleaching could result in a decrease in antibiotics secreted by symbiotic microorganisms, thereby causing the coral to become more susceptible to bacterial infection. This is in agreement with Ritchie (2006) who demonstrated that bacterial-produced antibiotics in coral mucus can regulate the coral microbial community.

Yellow blotch disease

Another disease that involves the disruption of the symbiosis between the coral animal and the endosymbiotic zooxanthellae is the yellow blotch disease that has been described on the major Caribbean reef-building coral *Montastrea* spp. (Cervino *et al.*, 2004a). During the early stages of the disease, a pale yellow blotch develops on the coral tissue, which eventually expands as the disease progresses. This paleness represents a decrease in chlorophyll concentration and a lack of symbiotic zooxanthellae. Four *Vibrio* spp., isolated from diseased corals, when inoculated onto healthy corals, either individually or as a consortium, caused disease signs similar to those of yellow blotch disease. Virulence of the *Vibrio* spp. increased with increasing temperature (Cervino *et al.*,

2004b). The authors conclude that the disease targets the zooxanthellae rather than the coral tissue.

Changes in microbial communities and disease signs in *O. patagonica* and the development of resistance of *O. patagonica* to *V. shiloi*

We have been studying the *V. shiloi/O. patagonica* model system of coral bleaching in the sea and in the laboratory for over 10 years. Sometime between 2002 and 2004, we found that the corals became resistant to the pathogen. The evidence for the development of resistance is based on the following (Reshef *et al.*, 2006):

- (1) From 1995 to 2002, the pathogen *V. shiloi* was readily isolated from 46/50 bleached and bleaching corals collected from the wild; from 2004 to the present, we have been unable to isolate *V. shiloi* from bleached or bleaching corals.
- (2) From 1995 to 2002, all laboratory strains of *V. shiloi* caused bleaching in controlled aquaria experiments; from 2004 to the present, none of the same strains bleached *O. patagonica* in the lab.
- (3) From 1995 to 2002, *V. shiloi* adhered to the corals, penetrated into the ectoderm and multiplied intracellularly to 10^8 – 10^9 cells per cm^3 ; now, *V. shiloi* adheres, penetrates the ectoderm and is rapidly killed.

Before the corals became resistant, the isolation and infection were so reproducible that for several years we used the system to demonstrate Koch's postulates in the teaching laboratory. Not only can we now not isolate *V. shiloi* from bleached corals but also molecular techniques fail to recover the 16S rRNA gene from ca. 1000 clones that were sequenced (Koren and Rosenberg, 2006).

Recently, Ainsworth *et al.* (2008) confirmed that *V. shiloi* is not currently present in bleached *O. patagonica*, using fluorescence *in situ* hybridization technology. However, the authors draw certain conclusions that are not justified by their data. To begin with, they claim the only microorganisms in close association with coral tissue were in the coral skeleton, an unusual conclusion considering the amount of mucus produced by the coral, and the abundant amount of coral-associated microbial sequences revealed by Koren and Rosenberg (2006) from colonies collected from the same sites. It is possible that due to the limitations of the fluorescence *in situ* hybridization techniques employed, these authors did not observe the presence of microorganisms in the coral mucus and gastrodermal cavity. Second, the fact that they were unable to observe any intracellular bacteria does not lead to the conclusion that bacteria are not the primary cause of bleaching. Many pathogens, especially those that produce toxins, do not grow intracellu-

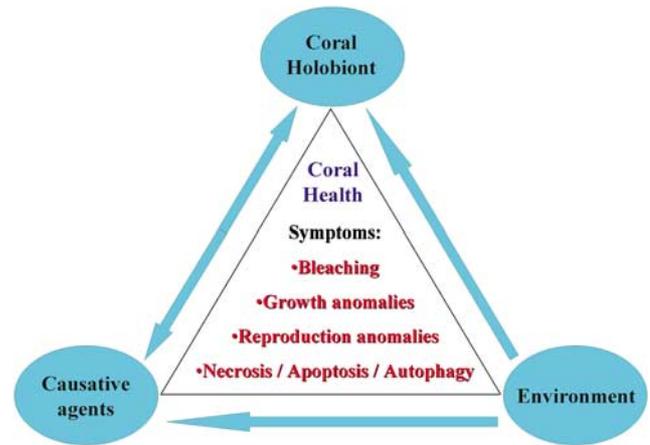


Figure 4 Disease is the result of multiple cues, including the environment, the causative agent and the host's susceptibility and the link among all of them.

larly. Bacteria that are present in the coral mucus or in the gastrodermal cavity could induce bleaching by this path. Third, they claim that the bleaching occurring in *O. patagonica* in the absence of *V. shiloi* occurs in the same manner as described earlier. However, this is not the case, the disease signs have changed significantly. Bleaching of *O. patagonica* begins in the spring when the temperature reaches ca. 25 °C (well below the 29 °C summer temperatures during the previous periods of bleaching in corals). In addition, the geographic distribution of bleached corals has changed and spread north along the coast (YL, unpublished results). But most convincing is the fact that in the past, the bleached corals did not develop gonads with ova and sperm (Fine *et al.*, 2002), whereas now they do (R Armoza, personal communication). These differences may be the result of the absence of the pathogen or of a change in the virulence factor, or of the development of an immune response, such as the release of host cytokines (for example, Mastroeni and Sheppard, 2004), or some combination thereof, though this warrants further study. Indeed, current research efforts are concentrating on understanding the differences in symptoms, causality and possibly novel causative agents.

The microbial hypothesis of coral bleaching and future research

Current understanding of disease etiology is that disease is the result of multiple cues, including environmental ones, that influence the causative agent (for example, to become virulent) and the host's susceptibility (Figure 4). There is no reason why coral diseases should not be investigated by applying the same principles.

Therefore, given that different abiotic and biotic factors can induce bleaching, the fundamental question remains: what is the etiology of patchy

bleaching and of mass bleaching that occurs periodically on coral reefs around the world? For this question, there are at least two different viewpoints. Most coral biologists take the position that high temperature and light act directly on the symbiotic algae to inhibit photosynthesis and produce reactive oxygen species, leading to bleaching (Jones *et al.*, 1998). According to this hypothesis, microorganisms play no role in the bleaching process and that changes in the microbial community of bleached corals are a result, not a cause, of the process. The second viewpoint, taken by certain coral microbiologists (including the authors of this review) is that high temperature acts on the coral microorganisms as well as on the coral host causing a change in the microbial community that in some cases contributes directly or indirectly to bleaching, that is, the microbial hypothesis of coral bleaching.

The microbial hypothesis of coral bleaching emerges from research spanning the last 10 years that has demonstrated that the coral holobiont is a complex and dynamic symbiosis involving the coral host, its endosymbiotic zooxanthellae and a large number and variety of accompanying microorganisms. In a healthy coral, the metabolic activities of each organism interact with the others to contribute to the growth, reproduction and disease resistance of the holobiont. For example, the coral animal captures prey, feeds on it and then the products of digestion may also provide nutrients for its associated microorganisms. The coral may also feed directly on its associated microorganisms (Kushmaro and Kramarsky-Winter, 2004). The algae perform photosynthesis that yields fixed carbon and oxygen that are major components needed for animal and bacterial respiration. When stressed, the symbiosis is broken down and the symbionts may be digested (Titlyanov *et al.*, 1996). Precisely how bacteria contribute to the holobiont is an area of current research. It has clearly been shown that some coral bacteria can fix nitrogen, others degrade complex polysaccharides and others produce antibiotics that may help prevent infection by pathogens. We postulate that coral bleaching results from a disruption of the equilibrium between the different components of the coral holobiont, resulting in a decrease in the endosymbiotic zooxanthellae.

Let us now consider how high light/temperature can affect the coral microbial community in a manner that leads to bleaching. As mentioned above, microbiological studies using both culturing and molecular techniques have demonstrated that increases in water temperature leads to a large decrease in some of the abundant coral bacteria and an increase in other bacterial species. Furthermore, the change in the bacterial community appears to occur prior to measurable bleaching (Bourne *et al.*, 2008). As it has been shown in man and other animal studies that the resident microbial community contributes to resistance to bacterial infection (for example, Silva *et al.*, 2004), it is

reasonable to assume that altering the coral microbiota can result in changes in resistance to infection. This is supported by the finding that during bleaching, corals lose their antibacterial properties (Ritchie, 2006).

The microbial pathogen(s) that cause the bleaching could come from sea water, through a vector, or from the resistant coral microbial community itself. In the latter case, we predict that the increased temperature would result in a much higher concentration of the pathogen and that virulent genes would be expressed. One possible virulence factor is a diffusible toxin, such as the toxin of *V. shiloi* that targets the algae rather than the coral tissue.

The microbial hypothesis of coral bleaching is testable. For example, do microorganisms which increase in number when the temperature is raised produce toxins that inhibit photosynthesis of the algae? Are such microbial toxins found in corals at the early stages of the bleaching event? In this regard, it would be interesting to test whether the *Vibrio* spp. that increased during the mass bleaching event on the Great Barrier Reef (Bourne *et al.*, 2008) synthesize toxins at the elevated temperatures.

It is important to keep in mind that certain pathogens have the capacity to cause disease only in a host under special conditions that favor the microbe. In the case of coral bleaching, increased seawater temperature can 'cause', in principle, bleaching by either inducing the microbe to be more virulent or the host to be more susceptible. Therefore, we would like to emphasize that the concept that bleaching is the result of high temperature acting on the zooxanthellae or on the bacterial community of the coral holobiont are neither mutually exclusive nor inclusive. It could be that both mechanisms act synergistically. It is also possible that other mechanisms are involved, such as temperature-induced virulence of certain viruses. Clearly, further multidisciplinary research including a combination of coral microbiology together with coral host physiology is required to clarify the coral bleaching disease process.

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