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HARMFUL ALGAL BLOOMS IN THE MEDITERRANEAN SEA: EFFECTS ON HUMAN HEALTH.

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SUMMARY

A harmful algal bloom (HAB) is defined as a bloom that has deleterious effects on plants, animals or humans. Marine algal toxins are responsible for an array of human illnesses associated with consumption of seafood or exposure to aerosolized toxins. The effects of algal toxins are generally observed as acute intoxications, whereas the environmental health effects of chronic exposure to low levels of algal toxins are, to date, only poorly documented and an emerging issue. Consumption of seafood contaminated with algal toxins can result in five types of seafood poisoning syndromes: paralytic shellfish poisoning, neurotoxic shellfish poisoning, amnesic shellfish poisoning, diarrhetic shellfish poisoning and ciguatera fish poisoning. The aim of this paper is to provide an overview on HAB-related issues in the Mediterranean Sea.

Introduction

Algae are unicellular microscopic plants that can be considered the foundation of life. An algal bloom develops in the marine or freshwater environment when excessive growth of these organisms takes place because of changes in that environment. A harmful algal bloom (HAB) is defined as a bloom that has deleterious effects on plants, animals or humans [1, 2]. Phytoplankton blooms, micro-algal blooms, toxic algae, red tides or harmful algae are all terms for these naturally occurring phenomena [3]. HABs can deplete the oxygen and block the sunlight that other organisms need to live, and some HABs release toxins that are dangerous to animals and humans. Marine algal toxins are responsible for an array of human illnesses associated with the consumption of contaminated seafood and exposure to aerosolized toxins. On a worldwide basis, marine algal toxins are responsible for more than 60,000 intoxication incidents per year, with an overall mortality rate of 1.5%. In addition to their effects on human health, algal toxins are responsible for extensive die-offs of fish and shellfish, and have been implicated in episodic mortalities of marine mammals, birds and other animals dependent on the marine food web. The impacts of algal toxins are generally observed as acute intoxications, whereas the health effects of chronic exposure to low levels of algal toxins are only poorly documented and an emerging issue [4, 5].

Algal toxins produced bydinoflagellates and diatoms also have an impact on humans. Filter-feeding shellfish, zooplankton and herbivorous fish ingest these algae and act as vectors to humans either directly (e.g. shellfish) or through further food web transfer of sequestered toxin to higher trophic levels. Consumption of seafood contaminated with algal toxins results in five seafood poisoning syndromes: paralytic shellfish poisoning, neurotoxic shellfish poisoning, amnesic shellfish poisoning, diarrhetic shellfish poison-

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ing and ciguatera fish poisoning. Most algal toxins are neurotoxins and all are temperature stable, so cooking does not ameliorate toxicity in contaminated seafood (Fig.1). In addition to foodborne poisonings, toxins from two dinoflagellate sources are aerosolized (brevetoxins) or volatilized (putative Pfiesteria toxin) to impact human health through the respiratory route. Over the past three decades, the occurrence of harmful or toxic algal incidents has increased in many parts of the world, both in frequency and in geographic distribution [6-8].

The predicted changes in our oceans are likely to impact interactions between humans and oceans both directly and indirectly. Recent studies have reviewed general oceanic responses to future climate changes, while acknowledging the impacts these changes will have on human societies [9-11]. Likewise, over the past decade, several studies have suggested possible relationships between climate and the magnitude, frequency, and duration of HABs [12].

Harmful Algal Blooms in the Mediterranean Sea and the Black Sea.

Dense blooms of phytoplankton are a widespread phenomenon of oceanic coasts worldwide. They develop in response to favourable conditions for cell growth and accumulation [13]. These blooms of autotrophic algae and some heterotrophic protists are increasingly frequent in coastal waters around the world. There is no doubt that HABs are occurring in more locations than ever before, and that new sightings are reported regularly. Several researchers have argued that this trend is due to increasing eutrophication throughout the world [14] but, generally, phytoplankton bloom has regional, seasonal and species-specific aspects that must be considered [15, 16]. In contrast to large-scale blooms that are dominated by mesoscale circulation, Mediterranean HABs are a more localized phenomenon, commonly related to areas of constrained dynamism, such as bays, lagoons, ports, beaches and estuaries (Fig.2). In these areas, enhanced growth of phytoplankton leads not only to a perceivable water discoloration along the shoreline, but also to a deterioration in water quality. Other unprecedented ecological effects in the Mediterranean area, such as fish death and risks to human health, have been attributed to toxic algal proliferations in recent years. Given that a bloom represents a deviation from the normal cycle of biomass, and despite the fact that in some cases the proliferation of algae may have a natural origin, coastal blooms are considered an emerging problem that could be related to nutrient enrichment of coastal waters. Intensive urbanization and recreational use of coastal watersheds has resulted in a remarkable increase in nutrient sources along the Mediterranean coasts. This cultural eutrophication generates a contrast between coastal waters and the open ocean where, due to summer stratification and nutrient depletion, oligotrophic conditions prevail in the upper layer. Nutrient-rich coastal environments of the Mediterranean Sea and, in particular, semi-enclosed areas with low turbulence levels constitute a new and unique environment in which several phytoplankton species with harmful effects may become dominant [17,18]. Even though most of the factors involved in the Mediterranean-near-shore algal outbreaks are known, the mechanisms that underpin their occurrence are not yet well established [19]. Along the coasts of North Africa, the spatial distribution of chlorophylls and carotenoids is attributed to the human-altered patterns of their physical structure and the nutrient concentrations, but also to the Modified Atlantic Water (MAW).

The physical forcing resulting from the MAW advection could confront distinct water masses and generate potential mixing of water from coastal and/or open ocean origin. This water mixing may have an impact on the phytoplankton populations, which, in North Africa, experience large variations in their abundance, composition and size structure due to the dynamic nature of their environment [20]. In the Black Sea, since the late 1970s, anthropogenic nutrient enrichment has been identified as a key ecological problem for this basin, especially its northwestern and western parts, which are mostly subjected to the influence of freshwater nutrient inputs. The input of nutrients and dissolved organic matter to the north-west shelf of the Black Sea by the Danube, the Dniepar and the Dniestar rivers increased about 10 times between 1950 and 1980. Increases in phytoplankton bloom frequency, involved species,

Year	Genus	Location	Source
Late 1960s	*Prorocentrum*	North Adriatic Sea	**Fonda Umani (37)**
1970s	*Noctiluca, Gonyaulax, Prorocentrum, Gyrodinium, Glenodinium,*	North Adriatic Sea	**Fonda Umani (37)**
1980s	*Katodinium, Noctiluca, Glenodinium, Prorocentrum, Gyrodinium, Gonyaulax, Scrippsiella, Massarthia*	North Adriatic Sea	**Fonda Umani (37)**
1984	*Gonyaulax*	Spain	**Shumway (38)**
1986	*Prorocentrum*	Black Sea	**Heil et al. (39)**
1989	*Gymnodinium*	Mediterranean Sea	**Shumway (38)**
1993	*Dinoflagellates*	Black Sea	**Bodeanu et al. (40)**
1995-1996	*Pseudo-nitzschia, Nitzschia, Cheatoceros, Ditylum, Cylindrotheca, Rhizosolenia, Heterocapsa, Protoperidinium, Scripsiella, Emiliana, Gonyaulax, Prorocentrum*	Black Sea	**Turkoglu (41)**
Since 1994	*Karenia*	Tunisia	**Marrouchi et al.(42)**
1994 and 1996-1999	*Alexandrium*	Spain	**Vila et al. (43)**
1994 and 1997	*Prorocentrum, Noctiluca, Erythropsidinium*	Greece	**Nikolaidis et al (44)**
1998	*Alexandrium*	France	**Masselin (34)** **Lilly (36)**
1998	*Chattonella*	Greece	**Nikolaidis et al (44)**
1999	*Prorocentrum*	France	**Heil et al. (39)**
1998, 2000, 2001	*Ostreopsis*	Tyrrhenian Sea	**Sansoni (45)**
2001	*Skeletonema, Cerataulina, Prorocentrum, Gymnodinium*	Black Sea	**Taylor et al. (46)**
2003	*Alexandrium, Gymnodinium*	Spain	**Basterretxea et al. (13)**
2000-2004	*Prorocentrum, Noctiluca, Gymnodinium, Alexandrium, Dinophysis, Pseudonitzschia*	Greece	**Nikolaidis et al (44)**
2005-2006	*Ostreopsis*	Ligurian Sea	**Mangialajo (47)**
2006	*Coolia*	Tunisia	**Armi et al. (48)**
2007	*Ostreopsis*	North Adriatic Sea	**Totti et al. (49)**
2010	*Ostreopsis*	Southern Italy	**ARPA Sicilia (50)**

Table 1: a series of HAB events during the last 50 years in the Mediterranean Sea and in the Black Sea [16].

duration, timing and area are well documented, provoking substantial perturbations in the entire food web structure and function. Changes in the structure of zooplankton communities and deterioration of benthic coenoses, culminating during the 1980s (a period of intensive eutrophication in the Black Sea), were to a great extent associated with the dramatic alterations in phytoplankton communities and recurrent hypoxic conditions. Microalgal blooms were therefore identified as one of the key issues for the ecological health of the Black Sea. Similar eutrophication problems have been identified in the Eastern Mediterranean Sea, within several Aegean and Ionian coastal areas affected by urban and industrial wastewaters and/or nutrient inputs from rivers and agricultural activities; thus phytoplankton, as the primary producer, became the first target of the anthropogenic-induced stress, resulting in dramatic alterations in species composition, abundance and biomass, seasonal dynamics and succession in the two basins [15].

Table 1 shows a series of HAB events in the Mediterranean Sea and the Black Sea [16].

Human health-related problems caused by or associated with the bloomings.

HABs can be harmful to human health in two fundamental ways: by inhalation of airborne toxins orconsumption of affected marine food resources.

Inhalation may occur when toxins released by several phytoplanktonic species become aerosolized after lysis or caught up in bubble-mediated transport. Bubble-mediated transport has been shown to concentrate toxins at the sea surface, where they are subsequently released as an aerosol. Terrestrial organisms, such as air-breathing mammals and reptiles, can be adversely affected by these aerosolized toxins. Also, blooms of some marine phytoplankton species (including cyanobacterium) cause a type of contact dermatitis (swimmer's itch) in humans swimming or bathing in affected waters. Symptoms include itching, rash, burning, blisters and deep skin erosions that can be very painful [22]. In Liguria (Italy), during 2005, more than 200 tourists and swimmers were hospitalized due to fever, cough, headache, nausea, conjunctivitis and dermatitis caused by coastal Ostreopsis ovata (Dinophyceae) blooms.

The impact of harmful microalgae is particularly evident when marine food resources, e.g. aquacultures, are affected. Shellfish and in some cases finfish are often not visibly affected by the algae, but accumulate the toxins in their organs. The toxins may subsequently be transmitted to humans, and through consumption of contaminated seafood become a serious health threat. Although the chemical nature of the toxins is very different, they do not generally change or decrease significantly when cooked; neither do they generally influence the taste of the meat. Unfortunately, detection of contaminated seafood is not straightforward, and neither fishermen nor consumers can usually determine whether seafood products are safe for consumption. To reduce the risk of serious seafood poisoning, intensive monitoring of the species composition of the phytoplankton is required in the harvesting areas, together with bioassays and/or chemical analyses of the seafood products intended for human consumption [23].

Given the large blooms, it is important to describe the adverse effects on human health ascribed to the marine toxin palytoxin after different exposure routes. Five human syndromes are presently recognized as to be caused by HABs: Amnesic shellfish poison (ASP), Ciguatera fish poisoning (CFP), Diarrhetic shellfish poisoning (DSP), Neurotoxic shellfish poisoning (NSP) and Paralytic shellfish poisoning (PSP). Table 2 summarizes the syndromes as well as theirproducer species, symptoms and treatment.

1. Human poisonings caused by palytoxin exposure.

Palytoxin (PTX) was first isolated from the zoanthid Palythoa toxica. Due to co-occurrence with other seafood toxins, such as ciguatoxins, saxitoxins and tetrodotoxin, it has been difficult to assess the true risk of PTX poisoning through seafood consumption in humans. However, limited cases have been well documented, some involving fatalities. Recent evidence also suggests that humans are negatively impacted by PTX exposure by inhalation and dermal contact routes [52].

The symptoms commonly recorded during PLX intoxication are general malaise and weakness, associated with myalgia, respiratory symptoms, impairment of the neuromuscular apparatus and abnormalities in

cardiac function. Systemic symptoms are often recorded together with local damage, whose intensity varies according to the route and length of exposure. Gastrointestinal malaise or respiratory distress is common for oral and inhalational exposure, respectively. In addition, irritant properties of PLX probably account for the inflammatory reactions typical of cutaneous and inhalational contact. Unfortunately, identification and/or quantification of the toxin are often incomplete or missing, and poisoning cases are indirectly ascribed to PLXs, according only to symptoms, anamnesis and environmental/ epidemiological investigations (i.e. zoanthid handling or ingestion of a particular seafood) [53].

2. Amnesic shellfish poisoning.

Amnesic shellfish poisoning is caused by consumption of shellfish that have accumulated domoic acid, a neurotoxin produced by some strains of phytoplankton. The neurotoxic properties of domoic acid result in neuronal degeneration and necrosis of specific regions of the hippocampus [24]. Human exposure to domoic acid occurs via the consumption of contaminated shellfish that have accumulated the toxin while filter feeding on toxigenic phytoplankton during blooms. The first reported human domoic acid poisoning event occurred in Canada in 1987; during this event clinical signs of acute toxicity such as gastrointestinal distress, confusion, disorientation, memory loss, coma and death were observed, and the illness was named amnesic shellfish poisoning (ASP). Due to effective seafood monitoring programs, no severe ASP cases have been documented since 1987. However, domoic acid poisoning has a significant effect on marine wildlife and multiple poisoning events have occurred in marine birds and mammals over the last few decades. Currently, domoic acid-producing diatom blooms are thought to be increasing in frequency worldwide, posing an increasing threat to wildlife and human health. Of particular concern are the potential impacts of long term low-level exposure in ''at risk'' human populations. The impacts of repetitive low-level domoic acid exposure are currently unknown [25].

The ASP syndrome is characterized by gastrointestinal and neurological disorders including memory loss. Gastroenteritis usually develops within 24 hours of the consumption of toxic shellfish; symptoms include nausea, vomiting, abdominal cramps and diarrhoea. In severe cases, neurological symptoms also appear, usually within 48 hours of toxic shellfish consumption. These symptoms include dizziness, headache, seizures, disorientation, short-term memory loss, respiratory difficulty and coma [26]. Mild human ASP intoxication is presently known to have occurred in many parts of the world [23,27] and several episodes have been reported in Spain, France, Greece and Italy, while there have been no reported occurrences in the Black Sea area to date [26].

3. Ciguatera fish poisoning

Ciguatera fish poisoning is a foodborne illness affecting humans worldwide. This illness is caused by the consumption of reef fish containing the naturally occurring ciguatoxins. Multiple ciguatoxins have been identified, but in this paper, ciguatoxins will be collectively referred to as "CTX." CTX is derived from the benthic dinoflagellates of the Gambierdiscus genus, growing predominantly in association with the macroalgae in coral reefs in tropical and subtropical climates. The toxin is transferred through the food web as the algae are consumed by herbivorous fish, which are consumed by carnivorous fish, which are in turn consumed by humans [27]. CFP produces gastrointestinal, neurological and cardiovascular symptoms. Generally, gastrointestinal symptoms such as diarrhoea, vomiting, and abdominal pain occur first, followed by neurological symptoms, including temperature sensation dysfunction, muscular aches, dizziness, anxiety, sweating and numbness and tingling of the mouth and digits. Paralysis and death have been documented, but symptoms are usually less severe although debilitating. Rapid treatment (within 24 hours) with mannitol is reported to relieve some symptoms. As there is no antidote, supportive therapy is applied, and survivors usually recover fully. However, the recovery time is variable among individuals and may take weeks, months, or even years. Absolute prevention of intoxication can only be obtained through complete abstinence from eating any tropical reef fish, since at present there is no method to routinely measure the toxins (ciguatoxin and maitotoxin) that cause ciguatera fish poisoning in any seafood product prior to consumption [28]. CFP is widely distrib-

uted in the tropics; in the period between 1960 and1984, there were a total of 24.000 cases of ciguatera poisoning in French Polynesia alone. Evidence shows that disturbance of coral reefs by hurricanes, tourist activity etc. increase the risk of ciguatera by providing more suitable habitats for the benthic dinoflagellates such as Gamberidiscus toxicus. Because of the tropic distribution of the causative species, so far CFP has never been documented in the Mediterranean Sea and the Black Sea.

4. Diarrhetic shellfish poisoning

Diarrhetic shellfish poisoning is a widespread type of shellfish poisoning which produces gastrointestinal symptoms, usually beginning between 30 minutes and a few hours after consumption of toxic shellfish with diarrhoea, vomiting and abdominal cramps. It is not fatal and the patients usually recover within a few days [23, 26]. There are thousands of reported incidents from developed countries, e.g. 5000 in Spain in 1981 alone, but with the pathological picture of DSP, many incidents may be regarded as an ordinary stomach disorder, and therefore remain unreported. Chronic exposure to DSP is suspected to promote tumour formation in the digestive system [26]. The first cases of contamination were detected in France in 1987. DSP contamination has also occurred along the eastern coast of Corsica [51].

5. Neurotoxic shellfish poisoning

Neurotoxic shellfish poisoning is a disease caused by the consumption of molluscan shellfish contaminated with brevetoxins; these are a group of more than ten natural neurotoxins produced by the marine dinoflagellate, *Karenia brevis* (formerly known as *Gymnodinium breve* and *Ptychodiscus brevis*) [29]. NSP produces an intoxication syndrome nearly identical to that of ciguatera, in which gastrointestinal and neurological symptoms prevail. In addition, the formation of toxic aerosols by wave action can produce asthma-like respiratory symptoms. No deaths have been reported and the syndrome is less severe than ciguatera poisoning, but nevertheless debilitating. Unlike ciguatera poisoning, recovery is generally complete within a few days [30]. Monitoring programs (based on K. brevis cell counts) generally suffice to prevent human intoxication, except when officials are caught off-guard in previously unaffected areas [23]. This syndrome has so far been restricted to the Atlantic coast of the US, Gulf of Mexico and New Zealand [29].

6. Paralytic shellfish poisoning

Paralytic shellfish poisoning is caused by naturally occurring potent neurotoxins synthesised by microscopic dinoflagellates from the genii *Alexandrium, Gymnodinium* and *Pyrodinium* in marine and freshwater environments [31]. Increased temperatures, sunlight and nutrient-rich waters are considered to trigger the rapid reproduction of dinoflagellate species and thereby lead to potential HABs. Climate change, increased ocean eutrophication and commercial shipping are believed to contribute to the increasing frequency and occurrence of these blooms worldwide [32]. PSP is a life threatening syndrome. Symptoms are purely neurological and their onset is rapid. Duration of effects is a few days in non-lethal cases. Symptoms include tingling, numbness, and burning of the perioral region, ataxia, giddiness, drowsiness, fever, rash and staggering. The most severe cases result in respiratory arrest within 24 hours of consumption of the toxic shellfish [33]. There is no known antidote to PSP. The known global distribution has increased markedly over the last few decades. Each year about 2000 cases of PSP are reported with a 15% mortality [23]. Many PSP cases have been reported in the Mediterranean Sea [34, 35, 36], but none in the Black Sea.

Conclusions.

This review of recent HAB research in the Mediterranean Sea area was focused on the potential health effects of exposure.

The complications and impacts of HABs are diverse, as are the causes and underlying mechanisms controlling the blooms. Pollution and other human activities in the coastal zone have increased the abundance of algae, including harmful and toxic forms. Seasonal monitoring and data collection in the Mediterranean Sea and the Black Sea should be encouraged.

Specifically, future research efforts should focus on developing empirical, theoretical and numerical simulation models to integrate observations, test and validate hypotheses, and generate risk forecasts of HAB occurrences and their impact on human health under future climate change scenarios.

	Paralytic shellfish poisoning (PSP)	Neurotoxic shellfish poisoning (NSP)	Amnesic shellfish poisoning (ASP)	Diarrhetic shellfish poisoning (DSP)	Ciguatera fish poisoning (CFP)
Causative organism	*Alexandrium andersoni, A. acatenella, A. catenella, A. cohorticula, A. minutun, A. tamarense, A. tamiyavanichi, Gymnodinium catenatum, Pyrodinium bahamense*	*Karenia brevis (=Gymnodinium breve); Pfiesteria piscicida* (neurotoxic), *P. shumwayae*	*Pseudonitzschia australis, P. delicatissima, P. pseudodelicatisima, P. Multiseries, P. fraudulenta, P. multistriata, P. pungens, P. seriata, Nitzschia navis-varingica*	*Dinophysis acuninata, D. acuta, D. caudata, D. fortii, D. mitra, D. norvergica, D. rapa, D. sacculus, D. tripos, Prorocentrum lima, P. arenarium, P. belizeanum, P. cassubicum, P. concavum, P. emarginatum.*	*Gambierdiscus australes, G. pacificus, G. polynesiensis, G. toxicus, G. yasumotoi Ostreopsis heptagona, Prorocetrum lima*
Symptoms in mild case	Within 30 min: tingling sensation or numbness around lips, gradually spreading to face and neck; prickly sensation in fingertips and toes; headache, dizziness, nausea, vomiting, diarrhoea.	After 3–6 h: chills, headache, diarrhoea; muscle weakness, muscle and joint pain; nausea and vomiting, paraesthesia; altered perception of hot and cold, difficulty in breathing, double vision, trouble in talking and swallowing.	After 3–5 h: nausea, vomiting, diarrhoea, abdominal cramps.	After 30 min to a few hours (seldom more than 12 h): diarrhoea, nausea, vomiting, abdominal pain.	Symptoms develop within 12–24 h of eating fish. Gastrointestinal symptoms: diarrhoea, abdominal pain, nausea, vomiting.
Symptoms in extreme case	Muscular paralysis; pronounced respiratory difficulty; choking sensation; death through respiratory paralysis may occur within 2–24 h after ingestion.		Decreased reaction to deep pain; dizziness, hallucinations, confusion; short-term memory loss; seizures.	Chronic exposure may promote tumour formation in the digestive system.	Neurological symptoms: numbness and tingling of hands and feet; cold objects feel hot to touch; difficulty in balance; low heart rate and blood pressure; rashes. In extreme cases, death through respiratory failure.
Treatment	Gastric lavage and artificial respiration. No lasting effects.		At this point, the treatment of ASP is symptomatic.	Recovery after 3 days, irrespective of medical treatment.	No antitoxin or specific treatment is available. Neurological symptoms may last for months or years. Calcium and mannitol may help relieve symptoms.

Table 1: A summary of syndromes, producer species, symptoms and treatment.

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Figure 1: Algal bloom event

Figure 2: Shellfish contaminated with PSP

Figure 3: Contaminated Shellfish warning in an affected area

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