RESEARCH

SYNTHESIS OF THE ENVIRONMENTAL, HEALTH AND TOXICOLOGICAL ISSUES

Parts Two

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Anthropic activities, amongst the countless benefits offered to humans, and which moreover have become essential, are unfortunately the cause of considerable changes in the ecosystem in its main sectors – air, ground, water – causing their widespread contamination and having an influence on global climatic conditions. The greenhouse effect in particular is the most worrying expression for the consequences already in course and those foreseeable for the future, as it is a cause of risk for the possible toxic effects on the various forms of life: plant, animal and human.
One phenomenon in particular summarises and is affected by all these negative effects that cause a global deterioration of the environment of which we are part, even if this phenomenon appears essentially in waterbodies: rivers, lakes and some seas. This is the eutrophication of waters, which was mentioned in the introduction; but not with reference to the "natural process" represented by the increase of nutrients in the waterbodies which is formed slowly over long periods of time, but the "cultivated" eutrophication, i.e. that very rapid phenomenon of human origin caused by the excessive introduction of nutrients into the aquatic system (Bruno and Melchiorre, 2000).
Legislative Decree no. 152 of 11th May 1999 (art. 2, letter t) gives the following definition:
"Eutrophication: enrichment of waters in nutrients, in particular of compounds of nitrogen and phosphorus which causes a proliferation of algae and superior forms of plant life, producing an undesired perturbation of the balance of organisms present in the water and in the quality of the waters concerned."
The undesired proliferation, referred to in the definition given above, is called blooms; this takes place in eutrophic conditions when one or two species of algae predominate for 80 – 90 % of the total of the phytoplankton composition, denoting a pathological condition of the aquatic environment. For example, the species of Cyanophyceae and Dinoflagellates (for example, of the Alexandrium genus) are considered to be eutrophic blooms when they exceed the values of 1 million individuals/litre and 20,000 individuals /litre respectively (Bruno and Melchiorre, 2000).
Algal blooms which can be defined as "physiological" can also be found in oligotrophic conditions but are generally composed of a great variety of genera in the context of the same class or division of algae (Bruno and Melchiorre, 2000).
There are three fundamental causes for the undesired proliferation of algae (Bruno, 2002):
- contamination of water bodies with excessive introduction of primary nutrients (phosphorus and nitrogen);
- the greenhouse effect that contributes to lowering the levels of the useful water supplies, causing a concentration of nutrients in specific seasons and encouraging the start of blooms;
- increased use of the sources of water with consequences similar to those described in the point above.

To this must be added the fact that algal blooms are often toxic. The adverse effects that are noted as a consequence of this are (Bruno and Melchiorre, 2000):
a – for the environment, in particular for the eutrophic waterbodies:
- excessive growth of superior aquatic plants;
- formation of algae foam or carpets of floating algae;
- release of bad odours due to the decomposition of the algae (geosmine and 2-methyl-isoborneol);
- formation of mucilage;
- formation of toxic marine aerosol;
- decrease in the transparency of the waters;
- deoxygenation of the deeper layers with production of sulphydric acid;

b – for the living organisms that come into contact:
- negative repercussions for human health, particularly as a consequence of the concentration of algae toxins along the food chain due to the accumulation of these toxins in the tissues of crustaceans, molluscs and fish of various sizes; human contact with the algae toxins also takes place by bathing in waterbodies with blooms in course or the use of water sources which are not perfectly potable;
- negative repercussions on the superior organisms present in the eutrophic system, with the extermination of fish, including on a generalized scale not only due to the deoxygenation of the waters, but also to possible algal toxins consumed;
- decrease in the fertility rate of some species of zooplankton.

If the supply of nitrogen and phosphorus is the reason triggering off eutrophication, this is also affected by other factors such as the extent and depth of the capacity, the time of turnover of the waters and the structure of the biotic community. Purely by way of example, table 3 shows in synthetic form some characteristics that differentiate an oligotrophic aquatic situation from a eutrophic aquatic situation; the quantitative criteria to assess the trophic state of a capacity of freshwater are, on the other hand, shown in Table 4.
In general, considering the various situations of danger that can occur as a consequence of the development of algal blooms in eutrophic conditions, the algal species concerned can be included in the following cases (Bruno and Melchiorre, 2000):
- Algal species that cause an innocuous colouring of the waters and that only exceptionally can develop so intensely as to cause large-scale deaths of fish and invertebrates at the time of their decline due to products of decomposition and the lack of oxygen in the aquatic medium, for example, Scrippsiella trochoidea.
- Algal species that produce powerful toxins that potentially can cause in humans a variety of gastro-intestinal and neurological syndromes, the typology and gravity of which are well described in literature; a synthesis is given in Table 5, which covers: Paralytic Shellfish Poisoning, PSP, caused by saxitoxin, neosaxitoxin, tetrodotoxin, gonyautoxins; Diarrhetic Shellfish Poisoning, DSP, caused by dinophysiotoxins (ocadic acid), pectenotoxins, macrolides (polyester lactones), yessotoxin and prorocentrolides; Amnesic Shellfish Poisoning, ASP, caused by domoic acid; Neurotoxic Shellfish Poisoning, NSP, caused by brevetoxins; ciguatera syndrome: ciguatoxins, gambierol, maitotoxin; contact dermatitis from aplysiatoxins; hepatotoxic effects from microcystins and nodularins and neurotoxic effects from anatoxin-a and anatoxin-a(S).
- Algal species that are not toxic for man, but harmful for fish and invertebrates due to damage of the branchial tissues; these are marine micro-algae called fish-killers, some of which have a surface covered in thorns (Congestri, 2000); the best known algae for their ichthyotoxicity are shown in Table 6.

All this leaves room for a series of considerations and recommendations to be borne in mind for further analysis in the forthcoming articles:
- eutrophication is often accompanied by toxic algal blooms, mucilage and aerosols;
- the significant production of algal biotoxins during blooms may cause extensive death of aquatic organisms, including by biomagnification, and neurotoxic, hepatotoxic, gastroenteric and allergic effects in humans who come into contact with them;
- the environmental fate of algal biotoxins has to be followed with great care as uncontrolled pollution may concern the entire aquatic chain both for drinking purposes and food technology uses and for other sectors;
- algal species producing toxins endemic in other countries can be implanted in Italian seas as they are transported by ships;
- the production and collection of algal species, for food purposes or other industrial purposes of transformation for the manufacture of derivatives and preparations for large-scale human consumption must be carried out in unpolluted areas and, in any case, checked for any appearances of toxic algal blooms;
- checks on drinking water, sea products

Table 3. Differential characteristics of oligotrophic waters and eutrophic waters (Bruno and Melchiorre, 2000).

Parameter or characteristic	Oligotrophic aquatic environment	Eutrophic aquatic environment
Production of aquatic plants and animals	low	high
Biomass	low and rare occurrence of algal bloom	high
Algal distribution	in the epilimnium and hypolimnium	only in the epilimnium
Daily migration of phytoplankton	considerable	limited
Oxygen dissolved in the hypolimnium	high levels all year round	low or nil
Conductibility	often low	high
Characteristic algal groups	Chlorophycae Desmidiacae (Staurastrum) Diatoms (Tabellaria) Chrysophycae (Dinobrion)	Cyanophycae (Anabaena, Aphanizomenon, Microcystis, Oscillatoria rubescens) Diatoms (Cyclotella, Melosira, Fragilaria, Asterionella)
Zooplanktonic species	Bosmina oblusirostris, Bosmina coregoni, Diaptomus gracilus	Bosmina longirostris, Daphnia cucullata
Fish	Salmonidae such as trout	Carp, perch, pike

Table 4. Criteria of classification of the trophy of internal waters (Bruno and Melchiorre, 2000).

Annual average values	Oligotrophy	Mesotrophy	Eutrophy
P_{total} (µg/L)	8	26.7	84.4
N_{total} (µg/L)	661	753	1875
Cl at µg/L	1.7	4.7	14.3
Cl at µg/L annual peak	4.2	16.1	42.6
Dry disks (m)	9.9	4.2	2.45

Table 5. Gastro-intestinal and neurotoxic syndromes and symptoms of poisoning caused in man by powerful algal toxins (Bruno, 2000; Bruno and Melchiorre, 2000; Dawson, 1998; Yu, 1995; Gallacher and Smith, 1999; Torigoe et al., 1988; Yu et al., 1998).

Algal species	Syndromes and symptoms	Algal toxins
Pyrrophyta: *Alexandrium acatenella* *Alexandrium catenella* *Alexandrium frundyense* *Alexandrium minutum* *Alexandrium fraterculus* *Marine dinoflagellates:*	**Paralytic Shellfish Poisoning, PSP** 100 - 200 cellules/litre of A. catenella are sufficient to cause an accumulation of PSP in molluscs. Light symptoms within 30 minutes: pins and needles or insensibility to the lips which gradually extends to the face and neck; irritation of the fingers and toes; headache, restlessness, acute gastroenteritis. Serious symptoms: muscular paralysis, pronounced respiratory difficulties, sensation of suffocation; death by respiratory paralysis may occur within 2-24 hours of ingestion. Treatment: gastric lavage and artificial respiration. Relaxants must not be given.	**Saxitoxin** It bonds to the sodium channels blocking the flow of the ion in and from the nervous and muscular cells. LD50 for Swiss mice = 10 mg/kg p.c. Lethal dose for man: 7 – 16 mg/kg; 1 – 2 mg by mouth. Admitted limit in Italy in molluscs: 80 µg/100 g. Neosaxitoxin Tetrodotoxin Gonyautoxins The last named are actually metabolites of Saxitoxin and neosaxitoxin.
Dinophysis acuta *Dinophysis acuminata* *Dinophysis fortii* *Dinophysis norvegica*	**Diarrhetic Shellfish Poisoning, DSP** 200 toxic cells of Dinophysis are sufficient to produce an accumulation of DSP in edible molluscs. Light symptoms from 30 minutes to a few hours (sometimes more than 12 hours): diarrhoea, nausea, vomiting, abdominal pain. Serious symptoms: chronic exposition promotes the formation of tumours in the digestive system. Treatment: hospitalisation especially after no response to medical care. Remission takes place on average after 3 days.	**Dinophysitoxins (ocadaic acid, DTX-1, -2, -3)** Similarly to microcystins, they inhibit the protein phosphatases PP1 and PP2a. Potent activity as tumoral promoters. if accompanied by the action of a carcinogen such as hydrocarbons. Limit of tolerance in molluscs: for ocadaic acid it is 40 mg/100 g; for DTX-1 it is of 36 mg/100 g. Pectenotoxins Damage to the cytoskeleton of the hepatocytes of chicken embryos with a reduction of the microtubules and loss of their radial architecture.. Reversible effect at doses < 0,5 mg/ml for 4 hours Macrolides Yessotoxin (seven similar) LD50 in the mouse = 100 mg/kg p.c. Prorocentrolides LD50 in the mouse = 400 mg/kg p.c.

Algal species	Syndromes and symptoms	Algal toxins
Pseudonitzschia pseudodelicatissima *Pseudonitzschia pungens var. multiseries* *Pseudonitzschia pseudoseriata (synonym of Nitzschia australis)*	**Amnesic Shellfish Poisoning, ASP** Light symptoms after 3 – 5 hours nausea, vomiting, diarrhoea, abdominal cramps. Serious symptoms: decreased reaction to profound pain, restlessness, hallucinations, confusion, short-term loss of memory. The result in elderly patients is often fatal. Treatment: under experimentation, for the time being only symptomatic	**Domoic acid** It bonds to the glutamate receptors of the kainate type on neurons of the hippocampus, causing a protracted depolarisation followed by degeneration and cellular death. The lesions of the toxin in the hippocampus cause the patognomonic symptom of memory loss. LD50 in the mouse = 3.6 mg/kg p.c.
Ptychodiscus brevis *(ora Gymnodinium breve)*	**Neurotoxic Shellfish Poisoning, NSP** In man there is depolarisation of the smooth muscles in the tracheal and bronchial tissues; the syndrome may simply take place by breathing (whilst bathing or a walk) the aerosol of the toxins during the bloom. The aerosol causes a dry cough, wheezy breathing, a sensation of burning of the conjunctives, lacrimation, rhinorrhea, sneezing and asthma attacks in predisposed subjects.	**Brevetoxins** They bond to the sodium channel but in a place other than that of the saxitoxin, causing an opposite effect. They are exciter agents, which produce a repetitive activation of the nervous axon.
Tropical benthonic Dinoflagellates : *Gambierdiscus toxicus* *Ostreopsis lenticularis*	**Ciguatera syndrome** The effects in man arise rapidly but are rarely fatal. The manifestations are of the neurological type (paresthesia and inversion of sensibility to heat), gastrointestinal (diarrhoea and abdominal pain) and cardiac (bradycardia, hypotension and sometimes tachycardia). Other symptoms include: weakness and dysuria, ophthalmological signs, cutaneous reactions, metallic taste, psychiatric disorders, polymyositis and polyneuropathies. In serious cases, there is oedema of the cytoplasm of the adaxonal Schwann cells with neuropathological symptoms.	**Ciguatoxin/s** They cause a permanent excitation of the neural axons. by means of repeated and continued activation. The site of the bond is identical with that of the brevetoxins. DL50 of ciguatoxin in the mouse = 0.45 mg/kg p.c. **Gambierol and maitotoxin** Other ciguatoxins of the family.
Tropical marine Oscillatobriacae: *Lyngbya maiuscola* *Lyngbya gracilis* *Schizotrix calcicola* *Oscillatoria nigroviridis*	**Contact dermatitis** Acute toxic effect: intense irritation after contact with the algae which evolves within 3-8 hours in a potent erosive dermatitis with a visible erythema on the exposed skin; this action is due to the attack of the toxic molecule on the receptor of phorbol, which is that of protein kinase C.	Chronic effect: activity of promotion of epithelial and gastrointestinal tumours such as that of the tetrahydrophorbol; this takes place by activation of protein kinase C. **Aplysiatoxins** **Debromoaplysiatoxin** They bond stably to the membrane receptor of protein kinase C. Lyngbyatoxin a
Cyanophycae	Light symptoms: nausea, vomiting, acute diarrhoea, headache, feverish state. Serious symptoms: even death in weak and debilitated individuals; chronic exposure to subacute doses promotes hepatic and epithelial tumours.	Microcystins or nodularins
Anabaena flos-aquae *Anabaena lemmermannii* *Anabaena circinalis* *Anabaena planctonica* *Oscillatoria sp.* *Aphanizomenon sp.* *Cylindrospermopsis sp*	Light symptoms: nausea, vomiting, diarrhoea, tingling in the lips, insensitivity. Serious symptoms: rapid generalized muscular paralysis, progressive respiratory difficulties, death.	Anatoxins: anatoxin-a homo-anatoxin-a (O. formosa Bory) anatoxin- A(S)

(fish, algae) of direct use, should include inspections for the absence of algal toxins;
- for imported products, the origin, nature, method of preparation and composition should be known; this is particularly important if we consider that the raw materials of algal origin and products based on algae which circulate in Italy are mainly from other countries, especially from the Far East.

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Table 6. Marine microalgae harmful for fish and invertebrates (Congestri, 2000).

Class	Genii and species	Bibliographic reference
Raphidophyceae (Chloromonadophyceae)	*Chattonella antigua* *Chattonella marina* *Fibrocapsa japonica* *Heterosigma akashiwo*	Toyoshima et al., 1989; Kawaino et al., 1996.
Prymnesiophyceae (Haptophyceae)	*Prymnesium parvum* *Prymnesium patelliferum* *Chrysocromulina polylepsis* *Chrysocromulina leadbeater*	Meldahl et al., 1995; Shilo, 1981. Meldhal et al., 1995.
Dinophyceae	*Gymnodium breve* [a] *Gymnodium mikimotoi* *Gymnodium nagasakiense* *Gymnodium pulchellum* *Gymnodium veneficum* *Gymnodium galatheanum* *Gymnodium sanguineum* *Amphidinium carterae* *Amphidinium klebsii* *Cochlodinium polykrykoides* *Alexandrium monilatum* *Alexandrium pseudogonyaulax* *Prorocentrum minimum* [b] *Pfiesteria piscidia* [c]	Dahl and Tangen, 1993. Larsen, 1994. Abbot and Ballantine, 1957; Nielsen and Stromgren, 1991). Yasumoto et al., 1990. Nagai et al., 1990. Yuki and Yashimatsu, 1989. Clemenson et al., 1980. Terao et al., 1990. Orlando et al., 1983. Steidinger et al., 1996.
Chrysophyceae	*Aureococcus anophageferens*	Tracey et al., 1990
Cyanophyceae d	*Nodularia spumigena* [d] *Hormothamnium enteromorphoides* *Synechoccus sp.* *Trichodesmium erythaeum* *Trichodesmium commersoni*	Francis, 1878. Gerwich et al., 1989. Skulberg at al., 1993. Feldmann, 1932; Endean et al., 1993.

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