

INTERNATIONAL SYMPOSIUM ON ALGAL TOXINS

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Piazzale Europa

Health problems after *Ostreopsis aerea* exposure in Italy



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Ostreopsis ovata and human health: what known?

- Data appear to be lacking regarding the effects on human health of *Ostreopsis ovata*.
- Some *Ostreopsis* strains produce a highly toxic compound known as palytoxin and analogues which can accumulate in fish and are implicated in clupeotoxism, associated with eating clupeoid fish. Environmental conditions and factors promoting palytoxin production are still largely unknown (Sanson et al 2003, Tanuyama et al. 2003, Usami et al. 1995).
- Palytoxin is one of the most potent non-peptidic marine toxins. It has a lethal dose to 50% of rats, mice, dogs and monkeys when given intravenously at ranges between 0.03 and 0.45µg/kg. It causes cytolysis as a result of the inhibition of Na⁺, K⁺-ATPase and has been recognised as the causative agent of fatal human seafood poisoning (Onuma Y et al. Toxin 1999, 4 Tosteson MT. Food Science and Technology Series 2000).

O. Ovata and human health: the recent italian experiences

- During recent years, some reports registered *Ostreopsis spp.* blooms occurring in the Tyrrhenian and southern Adriatic Sea have been related to human health problems, such as breathing and skin irritation, in tourists attending the beaches and inhaling marine aerosols. (Sansoni G et al. *Biologia Ambientale* 2003, Di Turi et al. *Biol Mar Medit* 2003, Gallitelli M et al. *JAMA* 2005, Ciminiello P et al. *Anal Chem* 2006, Brescianini C et al. *Eurosurveillance* 2006).
- Some authors had previously described other *Ostreopsis species* algal blooms along the Tyrrhenian coast, suggesting similar symptoms in exposed persons (Tognetto L et al. *Botanica Marina* 1995, Sansoni et al. 2000).
- The symptoms associated with *O. ovata* blooms in most of the affected Italian Regions are quite similar to those observed in the United States (Florida and other areas of the Gulf of Mexico), but the events in the United States have been associated with blooms of another algae, *Karenia brevis*, which produces brevetoxins (Mini-monograph: brevetoxins. *Environ Health Perspect* 2005; **113** (5): 618-657).

1: [JAMA](#). 2005 Jun 1;293(21):2599-600.

Erratum in:

JAMA. 2005 Jul 6;294(1):44. Silver, Nicolò Gentiloni [corrected to Silveri, Nicolò Gentiloni].

Respiratory illness as a reaction to tropical algal blooms occurring in a temperate climate.

[Gallitelli M](#), [Ungaro N](#), [Addante LM](#), [Procacci V](#), [Silveri NG](#), [Sabbà C](#).

PMID: 15928279 [PubMed - indexed for MEDLINE]

- During 2003 (mid-August, 7 days) and 2004 (early September 5 days) 2 microalgal blooms of *O. Ovata* occurred along the coasts of Bari, Italy.
- Twenty-eight cases (9 men, 18 women, and 1 child; mean age, 38.6 years, 10-68 years) presenting symptoms such as copious watery rhinorrhea, dry or mildly productive cough, fever to 38°C and bronchoconstriction with mild dyspnea were identified in subjects exposed to marine aerosol during recreational or working activities on the beach.

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*“.....Although there was no experimental challenge of healthy volunteers exposed to marine aerosol with or without *Ostreopsis* blooms or isolation of a putative palitoxin, complaints occurred concurrent with the algal blooms and disappeared when the *Ostreopsis* population decreased.*

Most symptoms improved or disappeared very rapidly when the patients left the beach.

It is likely that the patients' symptoms were related to the algal proliferation.....”

***Ostreopsis ovata* algal blooms affecting human health in Genova, Italy, 2005 and 2006**

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In mid July 2005, clinical-epidemiological and local environmental investigations were started following the first warnings of an unusual number of people needing care in several city Hospital Emergency Rooms (E.-R.s) in Genoa, after recreational or working activities on the beach.

Symptoms registered in more than 200 patients who attended E.R.s were rhinorrhoea, cough, fever, bronchoconstriction with mild breathing difficulties, wheezing, and, in a few cases, conjunctivitis.

Clinical-epidemiological investigation on human cases: case-definition of “algal syndrome”

A **clinical-epidemiological case-definition** was achieved following collection of the most significant anamnestic and clinical data obtained from the patients, including:

- those who had been by the seaside (<300 ft from the shore-line) and who needed care in an E.-R.

presenting with the association of at least two of the following symptoms:

- cough
- dyspnea
- pharyngeal pain
- rhinorrhea
- fever $\geq 38^{\circ}\text{C}$
- headache
- lacrimation
- nausea/vomiting
- dermatitis

Materials and Methods

Clinical-epidemiological data were collected by MDs, during the outbreak, from patients with attendance to the E.R. Hospitals who matched the above described case-definition, using both hospital clinical diaries and an “ad hoc” questionnaire .

All information was collected concerning:

- demographics
- date of onset of symptoms
- co-morbidity conditions (i.e., asthma or rhinitis)
- activities performed
- exact amount of time spent on the beach.



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Definizione di caso: soggetto che, nel periodo dal 17 luglio 2005, dopo aver soggiornato sulla costa del litorale genovese e in particolare dopo aver frequentato luoghi di balneazione, si sia presentato al D.E.A. di un Ospedale cittadino con un quadro clinico caratterizzato dalla presenza di almeno due dei seguenti sintomi o segni: febbre $\geq 38^{\circ}\text{C}$, tosse o dispnea, faringodinia, rinorrea, lacrimazione, cefalea, rash cutaneo, nausea e vomito.

Identificativo
(prime 2 lettere cognome e 2 nome).....

.....
Data.....Età.....Sesso.....

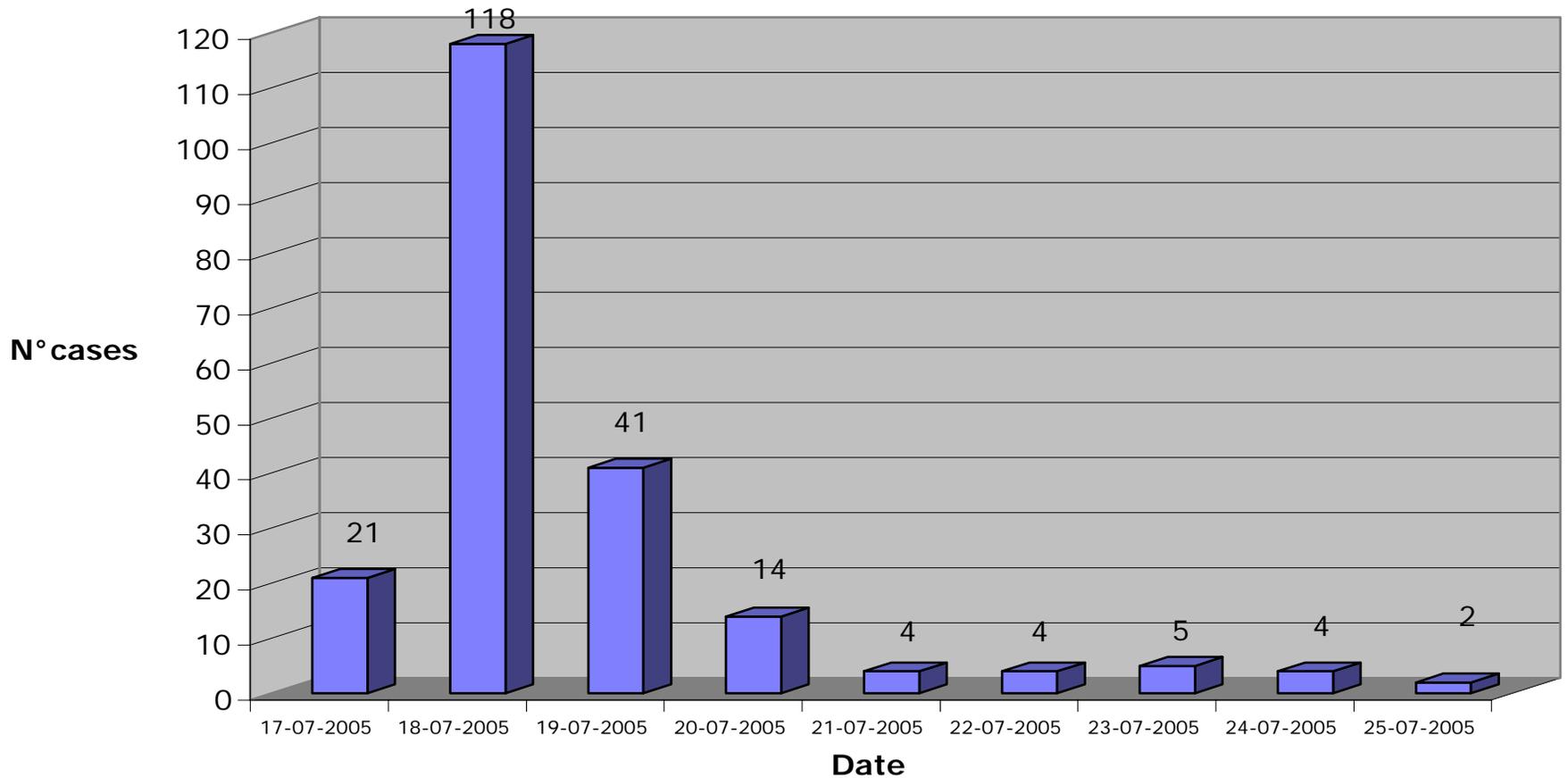
Sintomi (elencare):
.....
.....

Durata della sintomatologia.....
Spiaggia di soggiorno a partire dal 17/7/2005.....
Tempo di permanenza.....
Tempo di latenza fra esposizione e manifestazione clinica.....

Familiari/amici presenti (CASI e NON CASI).....
.....
.....

Balneazione	SI NO
Altre attività (elencare):
.....
Fattori preesistenti (barrare la patologia)	<input type="checkbox"/> Asma <input type="checkbox"/> Rinite <input type="checkbox"/> Dermatite atopica
Esami di laboratorio (fuori norma)
.....
Diagnostica strumentale: rilievi patologici
.....

Epidemic curve of patients affected by the “algal-syndrome” during 2005 season





***Ostreopsis Ovata* and human health: epidemiological and clinical features of respiratory syndrome outbreaks from a two-year syndromic surveillance, 2005-06, in North-West Italy**

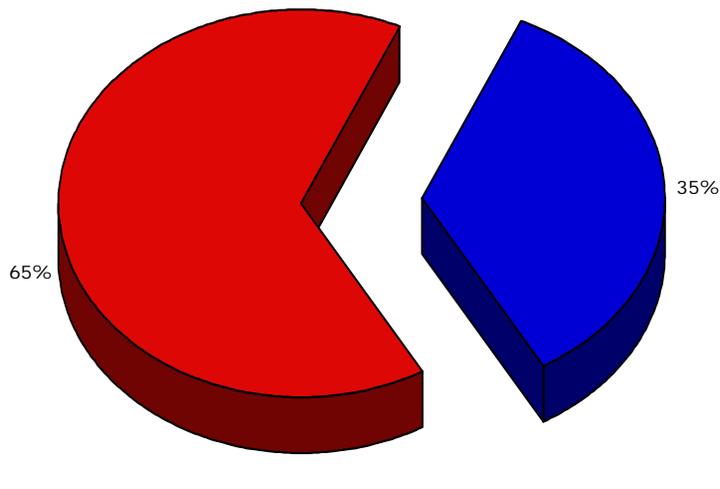
Durando P., Ansaldi F., Oreste P., Moscatelli P., Marensi L., Grillo C., Gasparini R., Icardi G.

(Euro Surveill. 2007, in press)

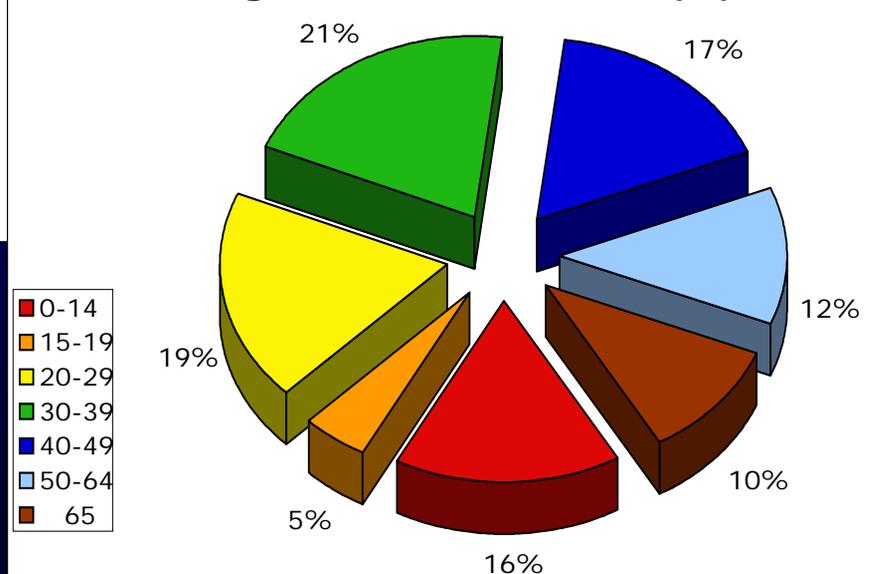
Sex and age distribution of the study population

Between July 17th and July 26th, 2005, 209 patients (73 males, 34.9%), mean age 35.9±20.1 years (range 1-89), matched the case definition.

Sex distribution(%)



Age-class distribution (%)



Clinical picture by symptom reported in 228 patients treated in hospital emergency departments in Genoa and La Spezia, during the summers of 2005 and 2006

	2005		2006	
	No.	%	No.	%
All patients	209		19	
Fever	133	63.6	6	31.6
Sore throat	105	50.2	7	36.8
Cough	84	40.2	14	73.7
<u>Dyspnea</u>	81	38.8	7	36.8
Headache	66	31.6	2	10.5
Nausea	50	23.9	3	15.8
<u>Rhinorrhea</u>	44	21.1	5	26.3
<u>Lacrimation</u>	33	15.8	1	5.3
Vomiting	21	10	1	5.3
Dermatitis	10	4.8	0	0

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Table. Characteristics and Symptoms of Patients Exposed to Tropical Algal Blooms

	No. (%)	Time of Onset After Beginning Exposure, Median (Range), h	Duration After Discontinuing Exposure, Median (Range), h*
Rhinorrhea	28 (100)	1 (0-3)	2 (0-10)†
Cough	12 (43)	2 (0-13)	3.8 (0.5-24)
Dyspnea and wheezing	7 (25)	8 (1-13)	12 (2-24)
Fever	4 (14)	10 (8-13)	24 (12-24)‡

*Median exposure duration (range) was 6 h (3 h-11 h).

†In 3 patients, rhinorrhea was markedly improved after 2 hours but persisted for the rest of the day.

‡Maximum temperature 38°C.

The most frequent associations of symptoms reported in 228 patients treated in hospital emergency departments in Genoa and La Spezia, during the summers of 2005 and 2006 (I)

	2005		2006	
	No.	%	No.	%
All patients	209		19	
PATIENTS WITH 2 ASSOCIATED SYMPTOMS:	80	38.3	18	94.7
Fever and sore throat	17	8.1		
Fever and <u>dyspnea</u>	7	3.4		
Fever and headache	7	3.4		
Fever and cough			5	26.3
Cough and <u>dyspnea</u>			3	15.8
Sore throat and <u>dyspnea</u>			2	10.5
Other associations	49	23.4	8	42.1
PATIENTS WITH 3 ASSOCIATED SYMPTOMS:	47	22.5	1	5.3
Fever, cough and sore throat	6	2.9		
Fever, cough and <u>dyspnea</u>	6	2.9	1	5.3
Other associations	35	16.7	0	0

The most frequent associations of symptoms reported in 228 patients treated in hospital emergency departments in Genoa and La Spezia, during the summers of 2005 and 2006 (II)

	2005		2006	
	No.	%	No.	%
All patients	209		19	
PATIENTS WITH 4 ASSOCIATED SYMPTOMS:	38	18.2	0	
Fever, cough, <u>dyspnea</u> and headache	5	2.4		
Fever, sore throat, headache and nausea	5	2.4		
Other associations	28	13.4		
PATIENTS WITH 5 ASSOCIATED SYMPTOMS:	24	11.5	0	
Fever, cough, sore throat, <u>dyspnea</u> and <u>rhinorrhea</u>	6	2.9		
Other associations	18	8.6		
PATIENTS WITH MORE THAN 5 ASSOCIATED SYMPTOMS:	20	9.6	0	
Fever, cough, sore throat, <u>dyspnea</u> , headache and nausea	5	2.4		
Fever, cough, sore throat, <u>dyspnea</u> , <u>lacrimation</u> and nausea	5	2.4		
Other associations	10	4.8		

Laboratory and instrumental exams

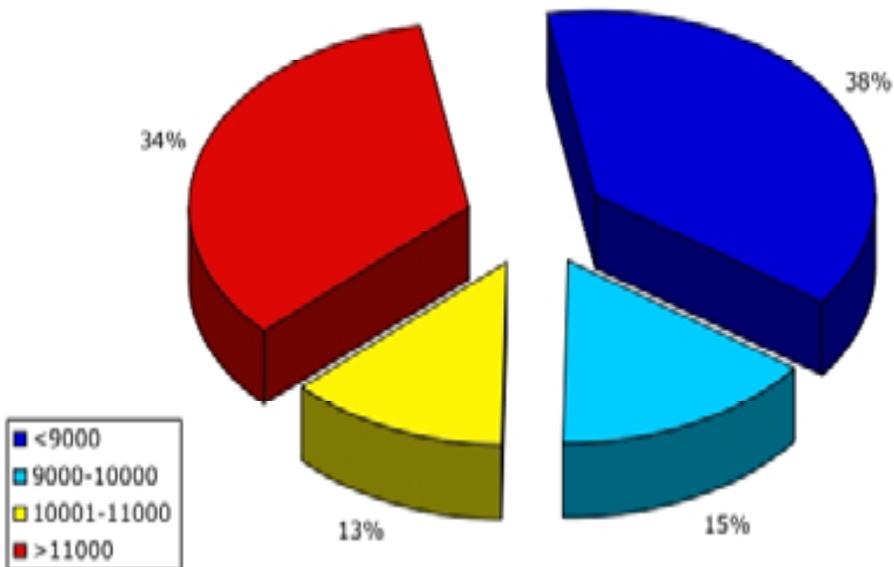
Laboratory analysis results were obtained during the acute phase in 82 (39.2%) patients:

The blood count showed leucocytosis (mean white cell count $13,900/\text{mm}^3 \pm 3,400$; range 10,100-23,900) and neutrophilia (mean $82.2\% \pm 4.7$; range 75.2-91.5) in 46.3% and 40.2% of the cases, respectively.

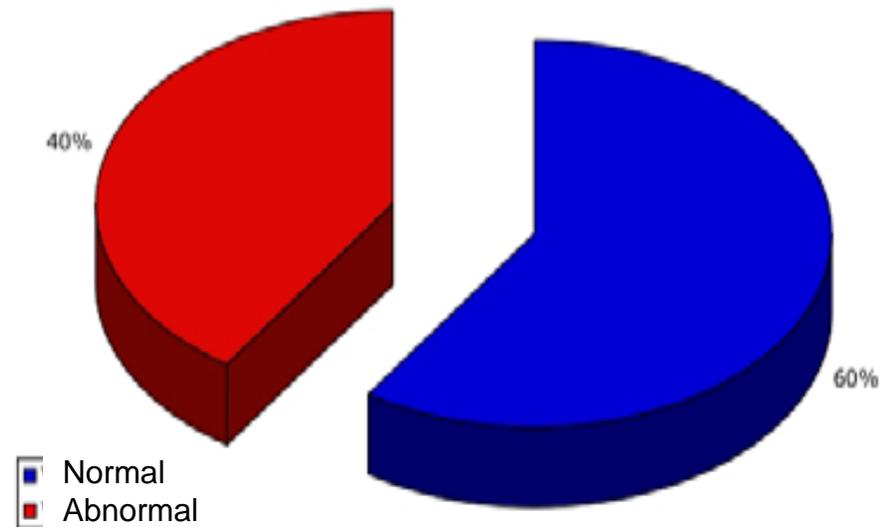
No other significant impairment of other biohumoral parameters was recorded (normal values of transaminases, gamma-glutamyl transpeptidase, creatinine and sedimentation rate).

All electrocardiographic examinations and chest-X-rays gave negative results.

White blood cell count: value-class distribution (%)



Neutrophilia: distribution(%) of cases by normal values



Anamnestic and Clinical picture: some highlights

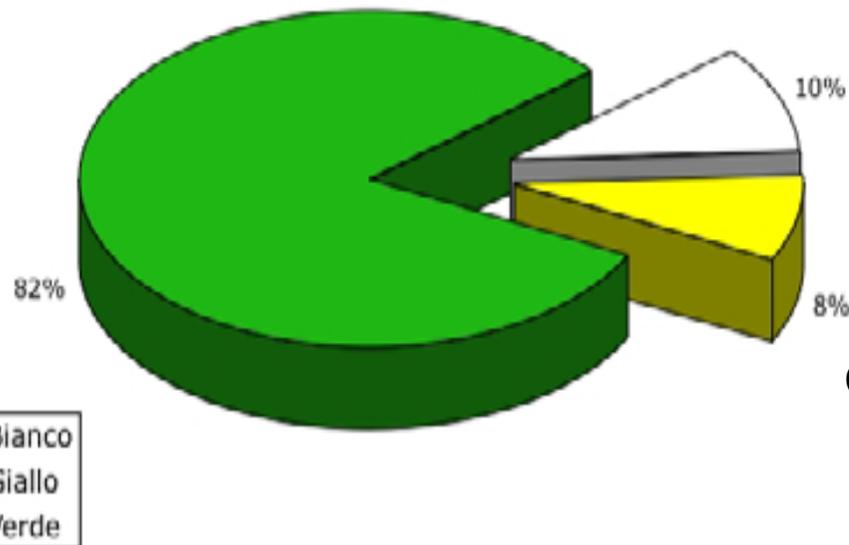
The most frequent symptoms were fever, sore throat, cough and dyspnea, variously associated

Mean onset of symptoms was 4h 33m (median 7h, range 30m-23h) after the beginning of exposure.

None of the risk variables (bathing, distance from the sea, length of stay on the beach, etc.) or personal and medical histories appeared to be associated with hospitalization.

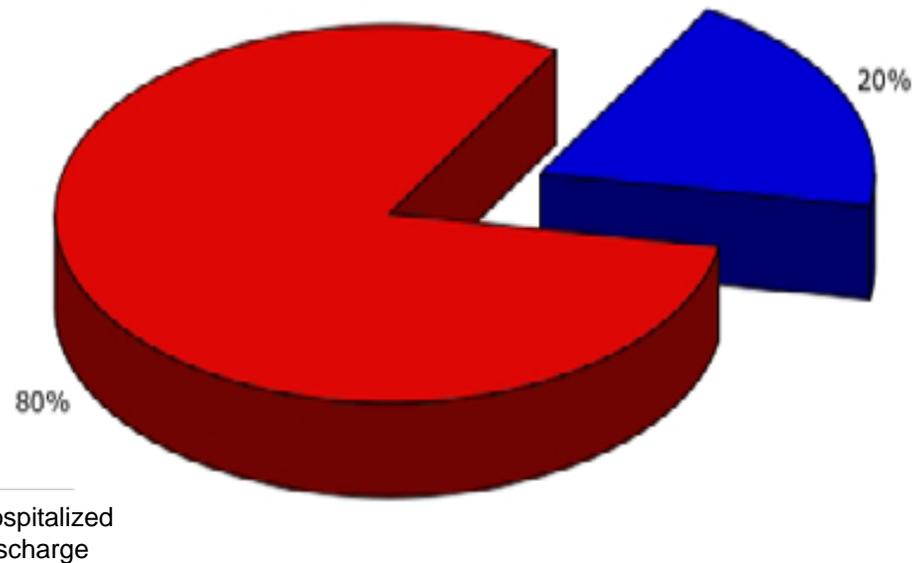
Clinical outcomes of the study population

Cases by Triage code (%)



Overall, 43 (20.6%) out of the 209 patients requiring access to E.R. needed hospitalization (hospital stay range 24- 72 hours).

Cases by hospitalization (%)



The most frequent associations of symptoms among patients requiring hospitalisation in Genoa, during the summer 2005

	2005	
	No.	%
Hospitalised patients	43	
PATIENTS WITH 2 ASSOCIATED SYMPTOMS:	11	25.6
Fever and sore throat	5	11.6
Fever and headache	4	9.3
Other associations	2	4.7
PATIENTS WITH 3 ASSOCIATED SYMPTOMS:	12	27.9
Fever, cough and sore throat	4	9.3
Fever, cough and <u>dyspnea</u>	3	7.0
Other associations	5	11.6
PATIENTS WITH 4 ASSOCIATED SYMPTOMS:	10	23.3
Fever, sore throat, headache and nausea	3	7.0
Other associations	7	16.3
PATIENTS WITH 5 ASSOCIATED SYMPTOMS:	6	14
Fever, cough, sore throat, <u>dyspnea</u> and <u>rhinorrhea</u>	2	4.7
Other associations	4	9.3
PATIENTS WITH MORE THAN 5 ASSOCIATED SYMPTOMS:	4	9.3
Fever, cough, sore throat, <u>dyspnea</u> , <u>lacrimation</u> and nausea	2	4.65
Other associations	2	4.65

Local environmental investigations

Just in the same days of the outbreak in humans, a concomitant superficial proliferation of macroalgal mucilage was described in the tract of the coast where the most cases have occurred.

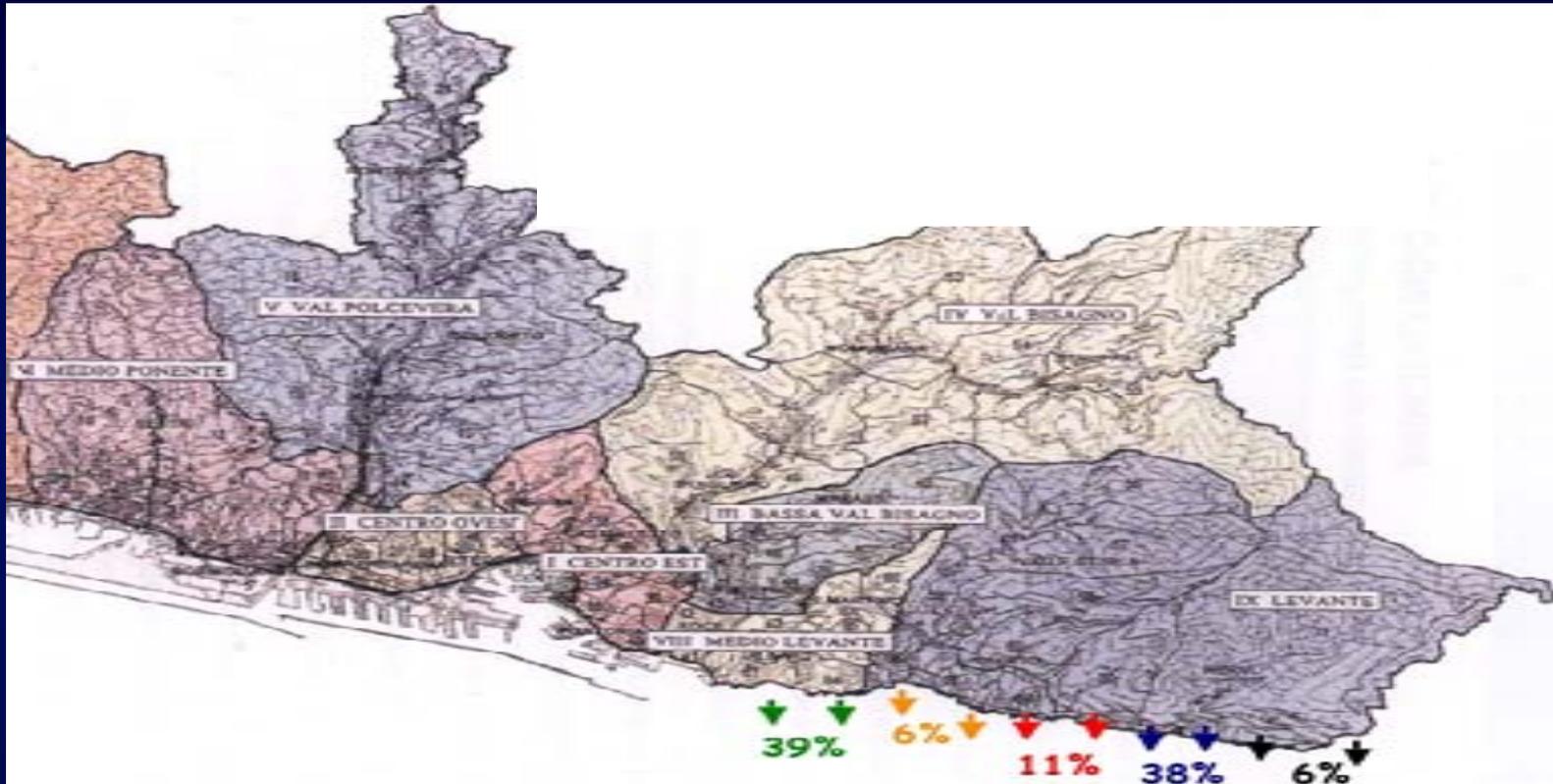
Local environmental protection staff immediately analysed air and water samples to exclude the presence of chemical pollution, and suspected a particular kind of unicellular alga, *Ostreopsis* spp, as a causative agent.

Sea water samples from around five beaches were taken for analysis every day in the first week after the outbreak, then twice a week and finally once a week. In the first days after the alert many samples were found to have high densities of *Ostreopsis ovata*, up to several thousands cells/l of sea water and hundreds of thousands of cells/g on macroalgae samples.

The analysis of water, plankton and macrophytae samples showed the presence of 'putative palytoxin' because the test could also have detected an isomer of palytoxin (Ciminiello P et al. [Anal Chem 2006](#))

After this bloom, *O. ovata* density dropped to much lower levels in a few days, and no further human health effects were recorded.

Space distribution of the cases along the coast and wheather conditions during the outbreak



An high water temperature and barometric pressure and a no windy meteorological condition, with a flat sea, in the days just before the first registered cases, matched with the peculiar typology of the coast with numerous small inlets, represent factors which have certainly favoured the algal bloom.

Public Health control measures adopted following the 2005 outbreak

- ✓ During 2005 outbreak, on the basis of the results of both the clinical-epidemiological and environmental investigations the Mayor of the city of Genoa, following the recommendations of the local Public Health Unit, suddenly ordered forbiddance of bathing along the tract of the coast interested by the outbreak.
- ✓ This safety precaution was adopted on 18th July, after the recognition of the outbreak, and went on for only 3 days due to the simultaneous resolution of the emergency for human health.
- ✓ The local Public Health Unit and the Regional Liguria Agency for the Environmental Protection faced the media, giving real-time informations to the population on both the developing situation and the Public Health preventive measures to adopt.
- ✓ An algal syndromic network, including the Regional Epidemiological Observatory, the main city Hospital E.-R.s and the local Public Health Units was set up and continued surveillance, throughout the summers of 2005 and 2006.

Management of the Public Health issues associated with *O. Ovata* blooms in Liguria, Italy

Regional Authorities
(Department of Health and Social Services Liguria Region)

City Authorities
(Municipality - Mayor)

Regional Agency for the Environmental Protection "ARPAL"

Liguria for the

Regional Epidemiological Observatory (Department of Health Sciences - University)

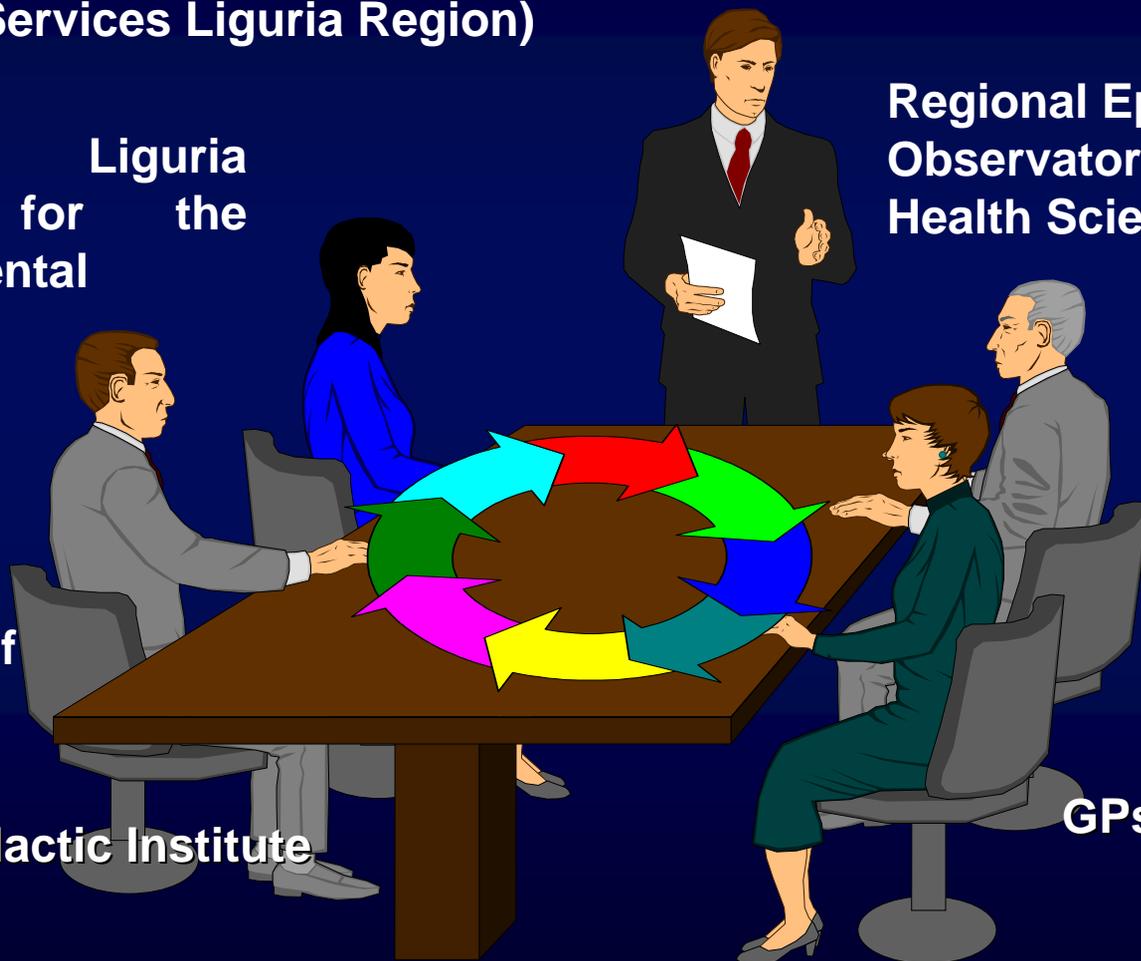
Local Health Agencies - Department of Prevention

City-Hospitals:
A.O.U. San Martino
E.O. Galliera
IRCCS Gaslini
.....

Zoo-prophylactic Institute

GPs, Paediatricians

Ministry of Health and NHI



***Ostreopsis Ovata* and human health: epidemiological and clinical features of respiratory syndrome outbreaks from a two-year syndromic surveillance, 2005-06, in North-West Italy**

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(Euro Surveill. 2007, in press)

During the next summer (July 29th-August 3rd and August 21st-23rd, 2006), 19 cases were suddenly identified by the surveillance network, following the above described case-definition, in the cities of Genoa and La Spezia.

On the basis of the experience of the previous year, the Genoese local Public Health Authorities ordered bathing to be forbidden (from 29th July to 4th August).

The anamnestic and clinical pictures of these patients were almost superimposable to that observed in the previous year but no patient required hospitalization.

	2005		2006	
	No.	%	No.	%
All patients	209		19	
PATIENTS WITH 2 ASSOCIATED SYMPTOMS:	80	38.3	18	94.7
Fever and sore throat	17	8.1		
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Other associations	35	16.7	0	0

Lesson learned from the recent experience and open issues (I)

- Worrying episodes occurred in Italy in the last years, describing humans affected mainly by respiratory symptoms after the exposure to concomitant *Ostreopsis Ovata* blooms, as in our experience, undoubtedly has opened the discussion on the urgent need to monitor and prevent such events.
- The importance of it is not simply related to an overriding Public Health issue but also to both social and economic aspects, strictly related to these phenomena.
- We support the hypothesis that *Ostreopsis Ovata* could have been the causative agent of these epidemics, mainly in consideration of the clear existing causative temporal criterion and by the exclusion of other plausible factors or conditions that have been investigated.
- Despite this, new studies focusing both the pathogenesis and the epidemiology of the disease but also the geographical distribution of the alga and its related favouring conditions to spread are necessary, also to identify new possible future preventive strategies.

Lesson learned from the recent experience and open issues (II)

The setting up of a syndromic surveillance network, including the Regional Epidemiological Observatory, the main city Hospital E.-R.s and the local Public Health Units could represent an efficacious tool for both the rapid detection of the sentinel-cases and health regulations by the Local Public Health Authorities, i.e. forbid bathing in the area, to limit the burden on human health.

The description of the clinical syndrome reported by patients exposed to *Ostreopsis Ovata* bloom could contribute not only to a better understanding of the effects of the exposure but also to the setting up of a more stringent case-definition for syndromic surveillance purposes.

Italian National Health Plan (2006-08)

5.8. Il controllo delle malattie diffuse e la sorveglianza sindromica

La sorveglianza sindromica

Allo stato attuale, la capacità di rilevazione tempestiva di eventi acuti singoli o epidemici, correlabili a emergenze di salute pubblica da determinanti naturali o dolosi, sembra inadeguata rispetto alla necessità che tale funzione sia sufficientemente diffusa ed organizzata in tutto il territorio nazionale.

Uno degli interventi per migliorare la capacità di identificare le emergenze di salute pubblica è l'attivazione di sistemi di sorveglianza sindromica che utilizzino dati prediagnostici tali da indicare gli stadi precoci di situazioni emergenziali. Questo tipo di sorveglianza integra, ma non sostituisce, il complesso dei molti sistemi di sorveglianza esistenti.

La sorveglianza sindromica va attivata prioritariamente nei servizi assistenziali dell'emergenza, come ad esempio i Pronto Soccorso e i Centri Antiveleni. Tra gli obiettivi prioritari si segnalano:

- la sperimentazione di un sistema informativo che permetta in tempo reale lo scambio delle informazioni tra i centri e la elaborazione dei segni prediagnostici (segni e sintomi) raccolti;
- la confrontabilità dei dati prediagnostici già esistenti, raccolti nei diversi servizi,
- la rilevazione tempestivamente dei quadri sindromici a partire dai dati prediagnostici;
- l'integrazione delle informazioni sui quadri sindromici con quelle provenienti da sistemi di sorveglianza già in uso.

Italian Guidelines for the assessment and management of the risk associated to *Ostreopsis Ovata* blooms

Linee guida

Gestione del rischio associato
alle fioriture di *Ostreopsis ovata*
nelle coste italiane

In order to deal with the problems due to blooms of marine algae, and especially *O. ovata*, the Italian Ministry of Health has set up an expert task force to chart the extent of the phenomenon and provide national guidelines.

Thank you for your
kind attention !!!