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## A regional approach to unmet needs in anaphylaxis

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### KEY WORDS

*Anaphylaxis; education; prevention; epidemiology; adrenaline*

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### Summary

*Allergic diseases are under-diagnosed and undertreated despite their wide prevalence, and particularly anaphylaxis is often under-estimated. Evidence-based anaphylaxis guidelines developed by principal allergy organizations agree on increased prevalence of anaphylaxis, especially in patients younger than 18 years (18-27,30): this trend highlights the need for actions on anaphylaxis management and prevention (3,4). Lack of prompt connection between emergency department and allergy unit after discharge, and of a dedicated ICD-9th identification code (18-26), can delay diagnosis and treatment of anaphylaxis (28,29). Also in the experience of our Allergy Unit, patients reach the allergist office after several attacks treated in ED (17), without a previous evaluation and risk assessment.*

*Keeping in mind unmet needs in anaphylaxis (4), we focused on regional approaches to health care delivery. The key point of our project was to establish an active collaboration between allergist clinicians and their counterparts in emergency medicine, with a system of quick filing report of patients discharged from ED with the suspect of anaphylactic reaction, directed to a central allergy unit, acting in a hub and spoke model with the Ligurian allergy network (31). Aim of the project was to improve epidemiological data collection via direct connection among ED and allergy network; moreover, we tried to provide a quick and proper evaluation of all reported patients, identifying, when possible, the agent responsible for anaphylaxis, to provide instructions on how to minimize future exposure; as all individuals at risk for anaphylaxis should carry and know how to self-administer epinephrine, we managed to provide auto injector and proper training when appropriate. A follow up on readmissions was carried out during the study and four months later.*

*In a 20 months observation period (2013/2014), 205 patients were reported: it was possible to reach a diagnosis and risk assessment in 64.3%. Anaphylaxis diagnosis was considered likely if any 1 of 3 criteria is satisfied within minutes to hours: acute onset of illness with involvement of skin, mucosal surface, or both, and at least 1 of the following: respiratory compromise, hypotension, or end-organ dysfunction; 2 or more of the following occur rapidly after exposure to a likely allergen: involvement of skin or mucosal surface, respiratory compromise, hypotension, or persistent gastrointestinal symptoms; hypotension develops after exposure to a known allergen for that patient: age-specific low blood pressure or decreased systolic blood pressure more than 30% compared with baseline.*

*Of 205 patients reported, 132 were classified as severe anaphylaxis; other 73 cases reported were 12 drugs related angioedema (mostly NSAID related), 9 ACEi related angioedema, 3 hereditary C1inh deficiency angioedema, 24 histaminergic idiopathic angioedema, 14 urticaria*

*angioedema, 6 severe asthma, 2 latex reactions; in three patients a proper diagnosis was not achieved due to refuse / impossibility to perform diagnostic workout.*

*Hymenoptera venom and food proved to be the main triggers, followed by drugs. 100% patients at risk of anaphylaxis received self-injectable adrenaline, pertinent education and individual action plan. In the same period, even though short, there were only two readmissions to ED. First result seems to confirm the usefulness of our approach to address some of unmet needs in anaphylaxis management, as recently pointed out by ICON guidelines (4).*

## Introduction

Italian National Health Service has a Regional organization. A regional approach to developing a health system strategy has to consider population base for the provision of high-quality services. Liguria is a small Region in Northern Italy, facing the sea, with a population of 1.600.000 inhabitants. Population density is 299 inhabitants / sqm. It seems to be an optimal population base over which to design emergency services (31). Genoa, capital city of Liguria, is endowed with two Research and Care Institutions, IRCCS San Martino, for adults, and IRCCS Gaslini, for children, and three medium size Hospitals; moreover, the region is divided in five distinct territorial districts, and other 6 smaller hospitals are distributed along the region. Regional HS is organized in a network of the main clinical, surgical and specialty areas. ED network consists of 19 locations situated in the main Hospitals. Medical Emergency Service (MES) works daily all over the regional territory, with 5 centrals and 18 medical stations. Allergy network is organized as a hub and spoke delivery model (31): the hub is Allergy Unit of IRCCS San Martino, main Hospital of Liguria Region, located in Genoa, in the center of the region; the spoke is represented by specialized staff in other 3 hospital units and 6 territorial units, distributed along the regional territory. All allergy specialists are connected through a dedicated social network, to share guidelines and clinical action. To address anaphylaxis unmet needs, Allergy Unit of San Martino proposed a common action: firstly all participants to allergy network agreed on EAACI and WAO anaphylaxis guidelines (9,10;1-4;6), and approved a diagnostic workout based on EAACI guideline regarding anaphylaxis, hymenoptera, food and drug allergy (5,10-16).

## Method

Once established as previously reported, the whole allergy network tried to increase the awareness of anaphylaxis and to disseminate anaphylaxis guidelines with their recommendations for management and prevention, using a comprehensive approach, among health professionals and caregivers involved. A common language with emergency network, as to say ED

and MES, by means of meeting, courses, digital and paper materials, and link to Scientific Associations sites was shared. All healthcare people, doctors and nurses, in ED, MES and allergy units, were involved as well. To reach global collaborations in anaphylaxis approach, GPs, PGPs and Pharmacists, as well as Allergic Patients organizations, have been involved with workshops. We shared EAACI and WAO guidelines (1,10) definitions of anaphylaxis as a “serious, generalized or systemic, allergic or hypersensitivity reaction that can be life-threatening or fatal”, the clinical features for a likely diagnosis of anaphylaxis, the usefulness of the term “anaphylaxis” instead of “anaphylactic shock” (1-3), the use of adrenaline as a first line intervention (4,9,10). To reach prompt initial anaphylaxis treatment an easy-to-follow and well-rehearsed protocol was proposed. We also focused on the need of an ICDM common code for anaphylaxis.

A simple report form, to send by mail to the central allergy unit (hub) immediately at pts discharge was agreed to, and provided (**table 1**).

Patients discharged from ED and reported, are contacted by the hub within 72 hrs, in order to plan an exhaustive allergic workout, performed in the Allergy unit nearest to the patient. The allergy testing was performed following guidelines, as reported (5). All patients with established diagnosis of anaphylaxis received a free epinephrine auto-injectors and personalized emergency action plans, allergen avoidance informations, and were trained with nurses. Moreover, pts received indication how to contact patient support groups. For long-term management of anaphylaxis we established review of EAI use training course at every epinephrine expiration data. Yearly follow-up with allergy specialist was planned. Help from nutritionists and psychologists was supplied when necessary.

All the anaphylactic patients reported to the hub and who met a diagnosis, are registered in a database. As soon as exhaustive allergic diagnosis and risk assessment were performed, a report was filed back to ED. An electronic flag, reporting “Anaphylaxis risk - Main trigger... - Provided with self-injectable adrenaline” was created and delivered to ED and MES; in case of recurrence, the flag shows up and gives the above informations.

*Table 1 - Anaphylaxis report form.*

**ANAPHYLAXIS REPORT FORM**

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18 (MES)   
  EMERGENCY DEPARTMENT   
  HOSPITAL   
  GPs PGP's   
  Pharmacists

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To send to the central allergy  
**osservatorio@hsanmartino.it**

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**SURNAME** **NAME**

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**DATE AND PLACE OF BIRTH**

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**TELEPHONE NUMBER**

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**Type of reaction:**

- Severe allergic reaction
- Anaphylaxis
- Other .....

**Allergy to:**

foods   
  drugs   
  insect sting   
  exercise induced anphylaxis   
  unknown

**Symptoms:**

URTICARIA   
  ANGIOEDEMA   
  VOMIT   
  BREATHLESS   
  LOSS OF CONSCIOUSNESS  
 DISPHONIA   
  DISPHAGIA   
  ASTHMA   
  ABDOMINAL PAIN/ DIARRHEA  
 PALMAR PLANTAR ITCHING   
  HYPOTENSION   
  SHOCK

**EPINEPHRINE THERAPY**

YES   
  NO

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The project had the aim to:

- prevent new admissions to the emergency department
- prevent fatal events
- provide every patient at risk for anaphylaxis with self-injectable adrenaline, education, action plan, medical ID stating triggers
- perform an exhaustive allergic workup, to reach an accurate diagnosis and risk assessment
- identify and report patients at risk to ED network
- perform continuing education for health professionals.

**Results**

A 20 month observation period shows 205 cases reported, 105 male and 100 female, median age anaphylaxis presentation is 42

(0 month - 85 years); in 132/205 (64.30%) anaphylaxis diagnosis was confirmed (**figure 1**); in other reports final diagnosis were: 6 severe asthma attacks, 62 angioedema (9 drug adverse reactions to ACEi, 3 HAE, 12 FANS, 14 urticaria - angioedema syndrome, 24 idiopathic) 5 unidentified trigger.

Among 132 with anaphylaxis, 81 were male (61%) and 51 female (39%) (**figure 2**). 88% pts had one or more previous ED access, only 11% pts had ED admission for the first time. In anaphylaxis established diagnosis, main triggers identified were (**figure 3; figure 4**):

- 55 hymenoptera venom, 1 horse fly;
- 53 food allergy;
- 15 with drug reaction, 1 radiological contrast medium;

- 2 with latex allergy;
- 3 exercise anaphylaxis;
- 3 unknown trigger (diagnostic workout was not performed due to impossibility / refuse to perform).

ED treatment:

- All pts received i.v / im steroids and antihistamine;
- 40% received adrenaline i.m.;
- post discharge treatment;
- 100% pts with established anaphylaxis due to hymenoptera and foods and (10% drugs) received Free Adrenaline autoinjectors;
- 33/54 hymenoptera venom allergic pts already started venom immunotherapy and desensitization; as it is recognized as lifesaving, Regional HS delivers it free of charge;
- 36/36 Food allergy pts have had risk assessment and dietetic advice;
- 16/16 drug allergy in order of frequency: NSAID (mostly ketoprofen and ibuprofen), amoxicillin-clavulanic acid, levofloxacin, cefazolin, ipp (lansoprazole), propyphenazone, tetracycline, cotrimoxazole;
- pts have been identified, when appropriate oral or cutaneous challenge have been performed. Adrenaline autoinjector was delivered, in consideration of risk of further reactions;
- in two years follow up time, during the study, only two emergency department readmission for a new severe allergic reaction were referred, one for nuts allergy, one for hymenoptera sting.

Figure 1 - Total pts reports versus anaphylaxis pts reports.

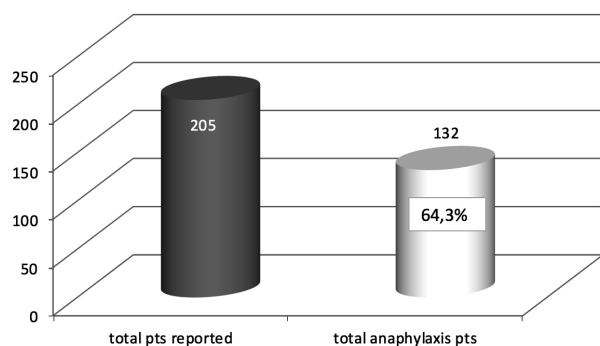


Figure 2 - Anaphylaxis: male and female.



Figure 3 - Total patients affected by anaphylaxis %.

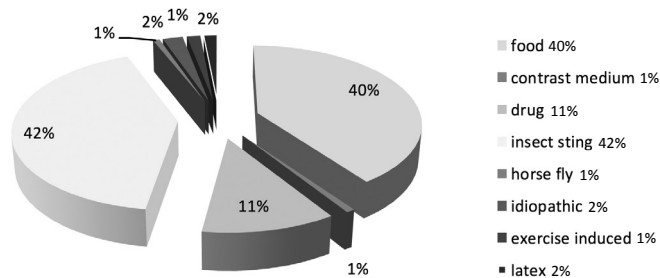
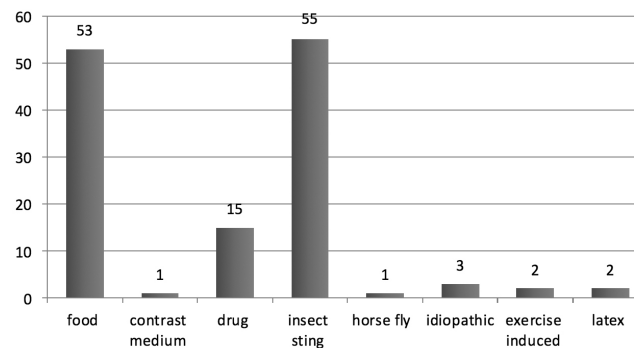


Figure 4 - Total patients affected by anaphylaxis.



Discussion

We try to address some unmet need in anaphylaxis management, as suggested in international anaphylaxis guidelines, focusing on “the supreme importance of making a prompt clinical diagnosis... Injecting epinephrine (adrenaline) intramuscularly” and “also emphasize preparation of the patient for self-treatment of anaphylaxis recurrences in the community, confirmation of anaphylaxis triggers, and prevention of recurrences through trigger avoidance and immunomodulation” and lack of epidemiological records (4).

Anaphylaxis is due often to reactions to medications, foods, and insect stings, but diagnosis can be challenging since it remains a clinical diagnosis, based on pattern recognition and probability. In our experience, cause and effect can be better evaluated in patients who experience anaphylaxis, if diagnostic workout is performed by the allergist soon after exposure to the causal agent. In our approach, cooperation among ED and the allergist guarantee a quick and proper evaluation of patients, providing comprehensive professional advice and instructions on how to minimize future exposure, suggesting specific preventive strategies, including pharmacologic prophylaxis and desensitization. Despite all individuals at risk for anaphylaxis should carry and

know how to self-administer epinephrine, and receive demonstration of proper self-administration technique with a placebo trainer auto injector, it is well known that many receive improper or no instructions; in our project, all patients received auto injector and training immediately after acute episode when appropriate, and retraining a some months after. Education, avoidance, and prevention of future episodes involved collaborative efforts between patients and health care professionals, since they are critically important in anaphylaxis management; the low number of ED readmission was encouraging, notwithstanding the observation time was short.

### Conclusion

These data confirm that “Prevention of anaphylaxis recurrences needs improved access to specialists, including those who can document sensitization to novel triggers”. Goal achieved in our project are the high number of anaphylaxis reported, with subsequent comprehensive diagnostic and therapeutic output, in our opinion due to training and to the quick reporting to prevent misdiagnosis. Moreover, it was possible to establish the offending trigger in 64.3% cases. Our results conflict with the perception that the disease is rare, and confirm the effectiveness of measures to prevent anaphylaxis recurrences. Our data contrast with epidemiologic reports in which anaphylaxis is described as rare. Connection among ED and allergy network enhance attention towards allergic severe reactions.

Further actions needed are:

- Reporting is incomplete from ED network (lack of anaphylaxis ICD9 specific code, carelessness, emergency first care units overcrowding, underrecognition, underestimation):
  - action needed: improve widespread dissemination of the protocol in all regional area;
  - action needed: improved training of healthcare professionals to identify anaphylaxis triggers, symptoms, and signs.
- Adrenaline is not yet a first line therapy:
  - action needed: improved training of healthcare professionals to identify anaphylaxis triggers, symptoms, and signs, and the usefulness of adrenaline.

In conclusion, Regional Health services implementation and development of anaphylaxis pathways has been proved as a good baseline for quality improvement, prioritization of anaphylaxis programs, and eventual reduction in morbidity and mortality. The system of surveillance and direct communication between ED network and Allergy network has led to acceptable results, although more is needed to strengthen the relationship and cooperation. Epidemiology needs integration of the clinical criteria for diagnosis of anaphylaxis with ICD-9 and ICD-10 codes; improving diagnosis by healthcare professionals and recognition by patients, caregivers, and the public,

will give reliable epidemiologic information about anaphylaxis and its prevalence.

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### Description of contribution

Paola Minale is the managing director responsible of the project, and wrote the article. Paola Dignetti collaborated to the recruitment of the pts, re-elaborated the records and collaborated to writing the article. Susanna Voltolini and Donatella Bignardi cooperated to the project. Costantino Troise Head of Allergy Unit IRCCS San Martino coordinated and supervised the project.

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