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Operative procedure for the monitoring of anaphylactic reactions and the prevention of recurrence

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Summary
Prevention of anaphylaxis depends on optimal management of patient-related risk factors, an educational programme to teach how to avoid confirmed relevant allergens.We observed in our routine practice several patients who underwent allergological evaluation months or years after the occurrence of anaphylactic reaction or a relapse. The main issues of this proposal are to identify all patients arrived to Emergency Unit with anaphylactic reactions ranging from Mueller classification grade II-IV and to refer them to an Allergy Unit with the intent to promote, within 48 hours, a diagnostic and therapeutic programme, set the anaphylactic risk for each patient and deliver Fast Jeckt (Epinephrine autoinjectors). The programme is evaluated by Quality Unit of Piacenza's AUSL that suggests two monitoring indicators: "Efficacy" of the plan is checked measuring recurrence rate in a year,"Quickness" of Allergological consultation is monitored recording time of consultation request from Emergency Unit and time of first allergological visit . We observe an increase in the number of patients referred to the Allergy Unit within 48 hours to receive a diagnostic and therapeutic programme to prevent recurrence of anaphylaxis: 6 patients in 2007 and 31 in 2010 and a decrease in the number of patients arrived after anaphylaxis sent by practitioner: 7 in 2007 and 1 in 2010 ($p < 0.05$) All quarterly reports have reported an Efficacy less than 15% of recurrences and a Quickness more than 90%. The procedure has received an institutional accreditation by Emilia Romagna Health Agency. These observations underline the importance of an operative procedure for the monitoring of anaphylactic reactions, in order to provide an effective and immediate medical examination and also avoid the risk of recurrence.

Anaphylaxis is currently defined as a severe allergic reaction that is rapid in onset and might be life threatening. Although the rate of occurrence is increasing especially in young people, anaphylaxis is likely to be under diagnosed, unrecognized or underreported for many different reasons. Only 1% of emergency department visits for acute systemic allergic reactions are classified as anaphylaxis.
The common triggers of allergic reactions are: hymenoptera stings (insects), foods, drugs, rubber latex, occupational allergens but also physical factors (cold air and water, heat, sunlight, after exercise) and idiopathic anaphylaxis.
Venom from stinging insects (Apidae, Vespidae, Formicidae) is considered in many studies as the most common cause of anaphylaxis; the rate of systemic reactions is 0,5%-7,1% (1).
An epidemiological study in Italy reported a prevalence of 0,34% in childhood and 2,7% in adults (2).

The rate of food allergy estimated in the USA is 3-4% in adults and 6-8% in childhood (3). The most common food triggers are peanut, tree nut, fish, shellfish, milk, egg, or food containing allergens such as lipid transfer protein. However there are significant geographical variations.
Another trigger of anaphylaxis is drug intake: 5% of patients visited in emergency department and 10-20% of patients in hospital suffered from adverse drug reaction (4). The most common drugs involved in adverse drug reactions are antibiotics (beta-lactams in particular), nonsteroidal anti-inflammatory (aspirin, paracetamol, ibuprofen), iodate contrast media, biological agents (monoclonal antibodies).
Some factors are important to perform appropriate risk assessment in individuals who have previously experienced an acute anaphylactic episode:

- understanding potential triggers;
- recognizing patient-related risk factors for severity and fatality (age, concomitant diseases such as uncontrolled asthma or mastocytosis, concurrent medications as angiotensin-converting enzyme inhibitors or beta blockers) (5);
- defining a clinical diagnosis in some cases confirmed by means of blood test (increase in serum tryptase level);
- confirming the triggers of anaphylaxis with a detailed history, skin test and specific IgE level in serum.

Prevention of anaphylaxis depends on optimal management of patient-related risk factors, an educational programme to teach how to avoid confirmed relevant allergens. All patients at risk for recurrence should be equipped with epinephrine autoinjectors (6, 7).

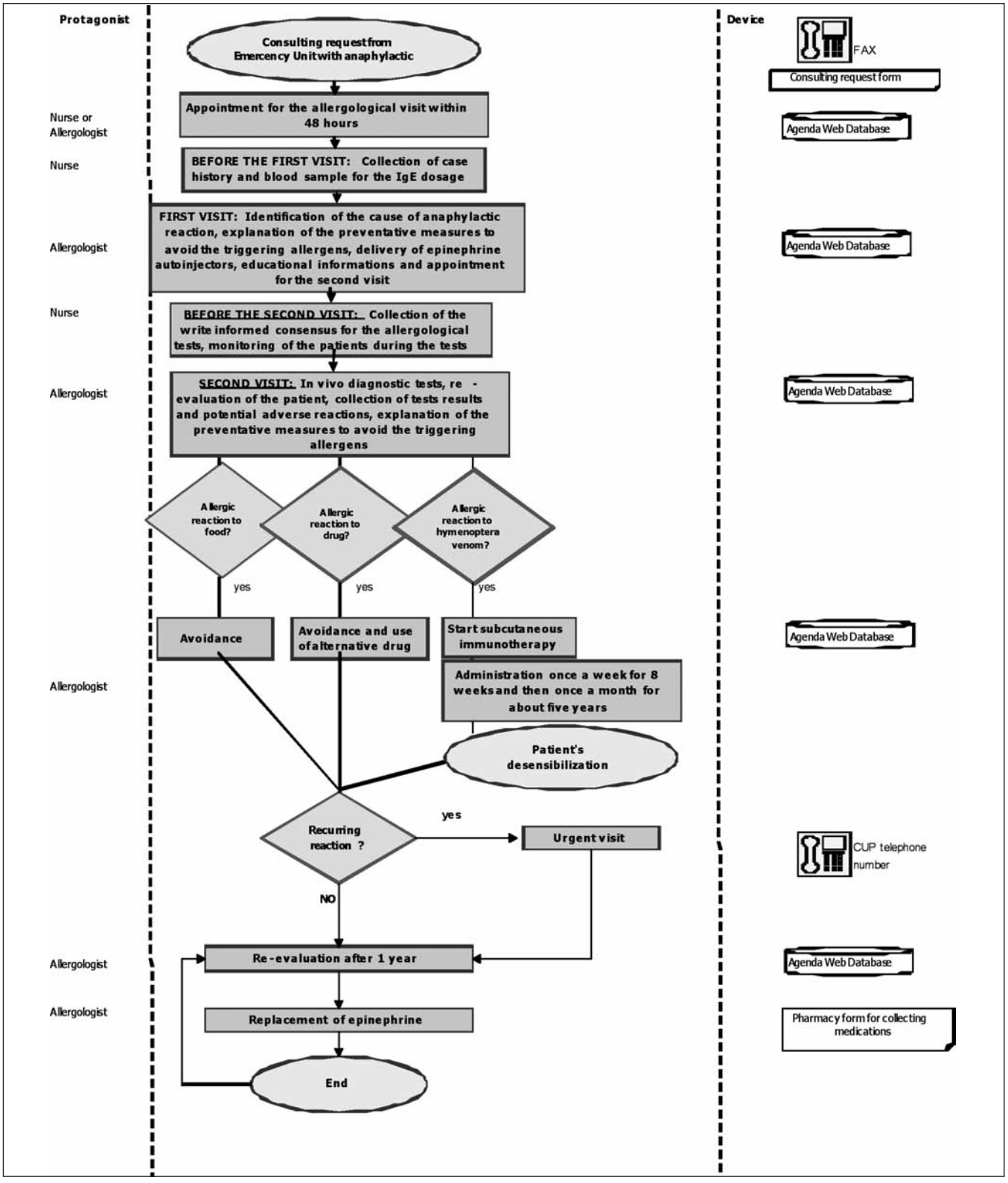
Programme's primary objective

We observed in our routine practice several patients who underwent allergological evaluation months or years after the occurrence of anaphylactic reaction or a relapse, or referred anaphylaxis during a visit due to other causes.
This is the reason why the main issues of this proposal are to identify all patients arrived at Emergency Unit with anaphylactic reactions ranging from Mueller classification grade II to IV and to refer them to an Allergy Unit with the intent to promote, within 48 hours, a diagnostic and therapeutic programme, set the anaphylactic risk for each patient and deliver Fast Jeckt (Epinephrine autoinjectors - the first choice treatment of anaphylaxis) supplemented by a written anaphylaxis emergency action plan. Moreover additional information measures are given, before the patients leave the hospital, to avoid other reactions: written personalized information to avoid triggers (food and its hidden sources, venom, drug, exercise). Clinical diagnosis of anaphylaxis can be confirmed by means of a blood test and skin test. Finally the programme is evaluated by the Quality Unit of Piacenza's AUSL that suggests two monitoring indicators: "Efficacy" of the plan is checked measuring recurrence rate in a year (that should be less than 15%); "Quickness" of Allergological consultation is monitored recording time of consultation request from Emergency Unit and time of first allergological visit (at least 90% of visits should be within 48 hours after the request).

Operative procedure for the monitoring of anaphylactic reactions

Since 2006, the Allergology Unit of Piacenza hospital has started an anaphylaxis protocol able to intercept all patients suffering from allergic reactions (Mueller classification grades II-III-IV) who reached the Emergency Unit of Piacenza, Castel San Giovanni and Fiorenzuola (Fig. 1).
These patients undergo a tryptase dosage within 4 hours after the reaction and an allergological consultation within 48 hours, before the discharge.
The Allergology Unit (an allergologist or a nurse) schedules an appointment for a visit within 48 hours after the request for consultation, received from the Emergency Unit by fax; the appointment is registered in the hospital's administration database, "Agenda Web".
When the patient arrives at the Allergological Unit, the nurse collects the patient's data and a tube of blood sample for specific IgE dosage, if the physician asks for it.
The Allergologist then visits the patient with the purpose of identifying the cause of the anaphylactic reaction, he/she then explains the preventive measures to avoid the triggering allergens and finally gives the patient the epinephrine autoinjector with all the educational information about how and when to use it.
The complete case history, diagnosis, grade of reaction, medications and preventive measures are recorded in the database together with the date of the new appointment for skin tests and the evaluation of in vitro tests.
During the second visit the nurse collects the written informed consent before carrying out the allergological tests and monitors the patient while skin tests are done.
The physician re-evaluates the medical history after examining the results of the tests (prick tests with commercial extract or fresh foods, prick tests and intradermal tests for drug reaction, oral provocation tests to identify alternative

Figure 1 – Operative Procedure



drug, prick tests and intradermal tests for hymenoptera venom allergy) carried out in accordance with guidelines.
Test results and potential adverse reactions during the diagnostic procedures are checked in the allergological database.
In light of the correct diagnosis, the Allergologist prescribes preventative measures and the specific immunotherapy, if necessary.
In case of recurring reactions or in any case after a year, the physician evaluates again the patient before providing him/her with a new epinephrine autoinjector (with expiration date of a year). This is accompanied by a form that contains patient's data and the triggering allergens and by a new explanation as to how to use the autoinjector.
Patients with hymenoptera venom anaphylaxis start a specific subcutaneous immunotherapy administered once a week for 8 weeks and then administered only once a month for about five years by the Allergologist. The patient must stay under observation for at least an hour after the injection. All the injections and the potential adverse reactions are recorded in the patient's diary.
In the flow chart reported below we describe the action plan, the responsibility of everyone, where the date are recorded and who records the date.

Indicators of quality

The Quality Unit of Piacenza hospital has identified as objectives to evaluate this course inter- departments: Efficacy and Quickness of intervention.
Numeric indicators have been chosen to evaluate the two objectives and the values of cut-off has been defined. In a periodic report are collected and recorded the date by the Reference of Allergology Unit and sends to Quality Unit (Tab. 1).
Efficacy is defined as a ratio:

- Number of recurrences of anaphylaxis/Total number of patients with grade II/IV anaphylaxis This ratio should be less than 15% for a good quality of the objective (data are reported in history case and "Agenda Web" and are evaluated the epinephrine autoinjectors delivered before the expiration date).

Quickness as defined as ratio:

- Number of patients with grade II/IV anaphylaxis treated by Allergological Unit within 48 hours/ Total number of patients with anaphylaxis. This ratio should be more than 90% for a good quality of the objective, the evaluation is based on analysis of Emergency Unit request's date and allergological consultation's date reported in database Agenda Web.

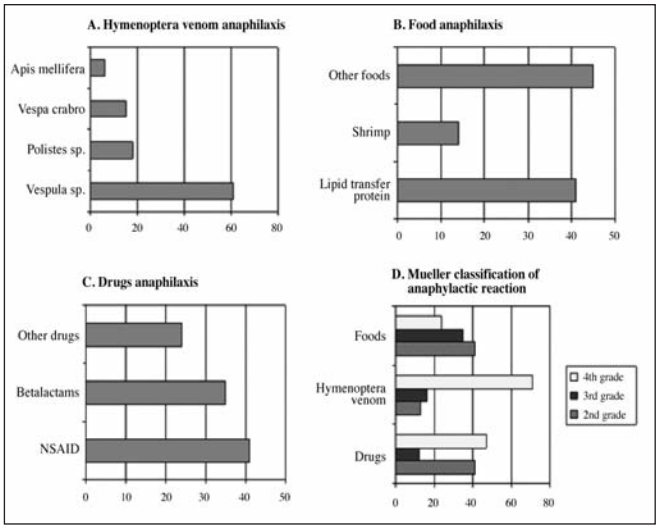
Table 1 – Indicators of Quality

Indicators	Who collects the data	Where the data are recorded	Time to sent the Report	Who evaluates the report
Efficacy	Nurse medical doctor	Data-base report-form o empty Fast-Jeckt, Agenda Web	Quarterly	Director Allergy Unit
Quickness	Nurse, medical doctor	Emergency Unit request's date, Allergological consultation's date in data-base Agenda Web	Quarterly	Director Allergy Unit

Table 2 – Reports 2007-2010

	2007	2008	2009	2010
Drug allergy	1	3	4	9
Hymenoptera venom allergy	4	4	18	12
Food allergy	1	6	2	8
Idiopathic reaction	0	1	1	2
TOT	6	14	25	31
Efficacy	0/6	0/14	0/25	0/31
Quickness	6/6	14/14	25/25	31/31

Figure 2 - Triggers and grade of Anaphylaxis



Results and conclusions

In this analysis we observe an increase in the number of patients referred to the Allergy Unit within 48 hours to receive a diagnostic and therapeutic programme to prevent recurrence of anaphylaxis: 6 patients in 2007 and 31 in 2010 (Tab. 2). In the same time we observed a decrease in the number of patients arrived after anaphylaxis sent by practitioner: 7 in 2007 and 1 in 2010 ($p < 0.05$).

These observations underline the importance of an operative procedure for the monitoring of anaphylactic reactions, in order to provide an effective and immediate medical examination and also avoid the risk of recurrence.

Despite the possibility of the absence of skin symptoms during anaphylactic reaction and the occurrence of an isolated cardiovascular shock as the only allergic manifestation, all the examined patients manifested also skin involvement. None presented Kounis Syndrome or cardiac involvement alone.

Hymenoptera venom is the most common trigger in our population with a rate of occurrence of 50%: *Apis mellifera* 6%, Vespula sp. 61%, Polistes sp. 18%, *Vespa crabro* 15% (Fig. 2A).

Foods are involved in anaphylactic reactions in a rate of 22%: Lipid transfer protein 41%, shrimp 14% and other 45% (Fig. 2B).

Drugs induce anaphylaxis in a rate of 22%: Antibiotics (beta-lactams in particular) 35%, nonsteroidal anti-inflammatory 41%, others 24% (Acyclovir, Methylprednisone, Macrolides) (Fig. 2C).

Idiopathic and other triggers are involved only in 5%.

Drugs induce Mueller grade IV anaphylactic reactions in 8 patients/17 (rate of 47%), hymenoptera venoms in 27 patients/38 (rate of 71%), foods allergy in 4 patients/17 (rate of 24%) (Fig. 2D).

All quarterly reports have reported an efficacy less than 15% of recurrences, the Quickness more than 90%. The procedure has received an institutional accreditation by Emilia Romagna Health Agency.

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