# Anaphylaxis

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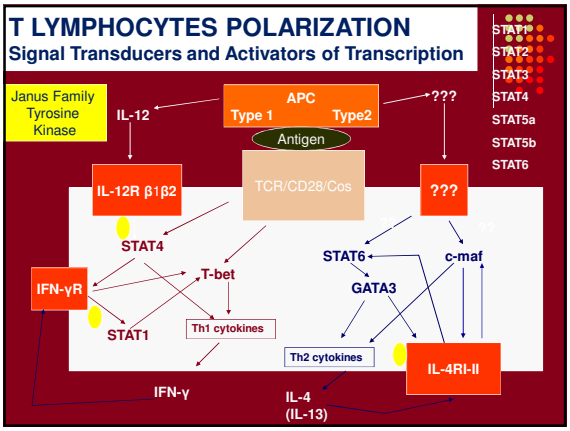
## T LYMPHOCYTES POLARIZATION

**Signal Transducers and Activators of Transcription**




## T LYMPHOCYTES POLARIZATION

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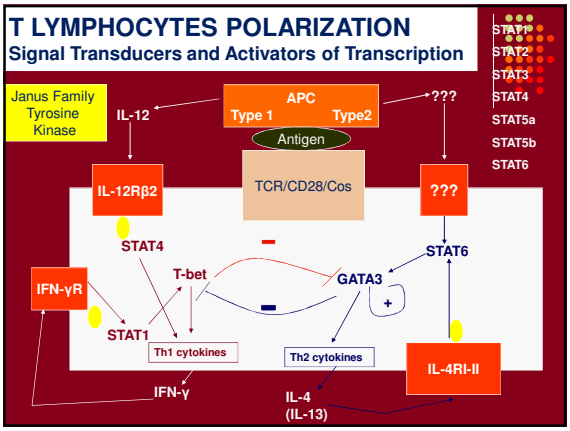
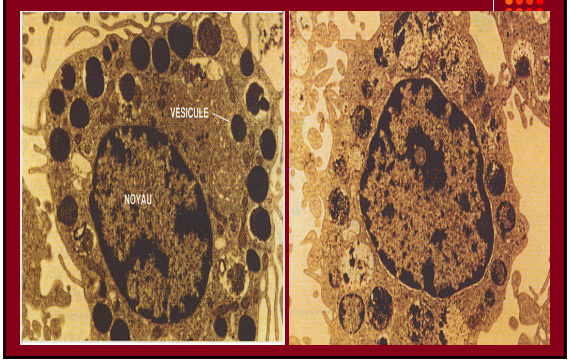
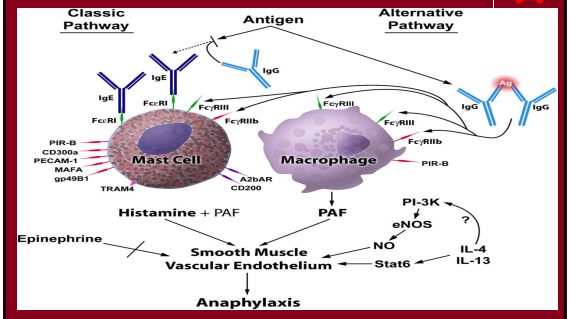



## MAST CELL

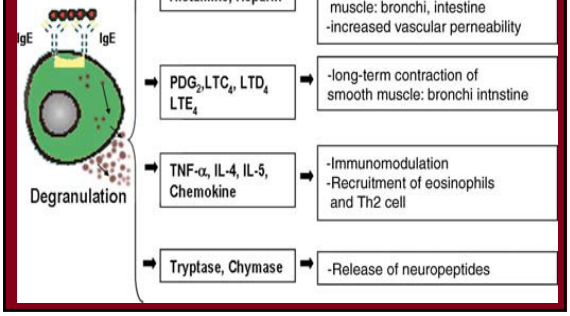



## Anaphylaxis

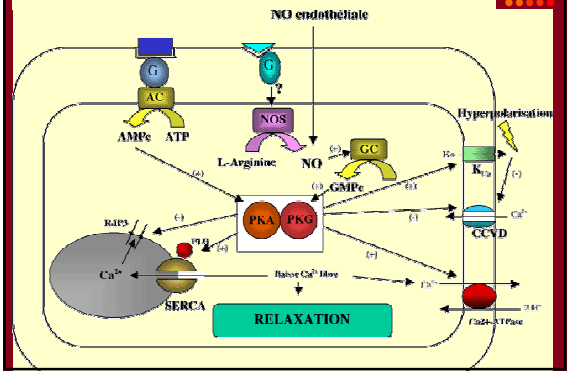



J Allergy Clin Immunol 2007;120:506-15

## MEDIATORS

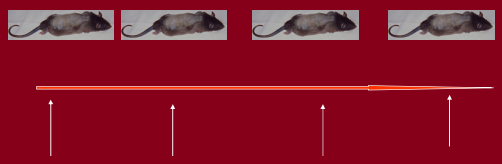



## Vasodilatation




## Anaphylaxis Rat Model

## Ovalbumin Allergy Model



J0 OVA+Al 1 mg SC

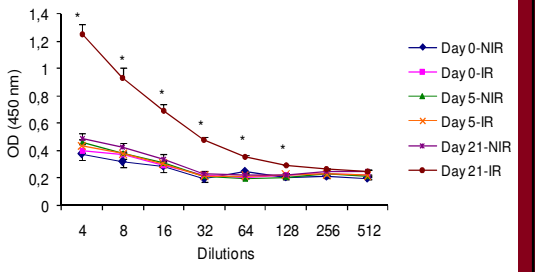
J5 OVA+Al 1 mg SC

J21 OVA+Al 1 mg SC

J28 SHOCK

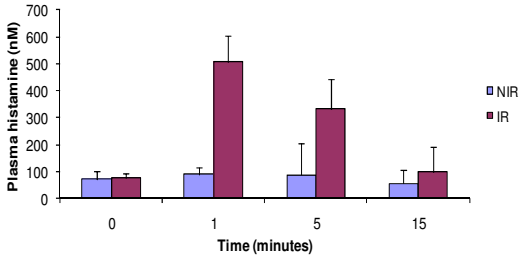
Scan J Immunol, 2003

## Production of OVA-IgE



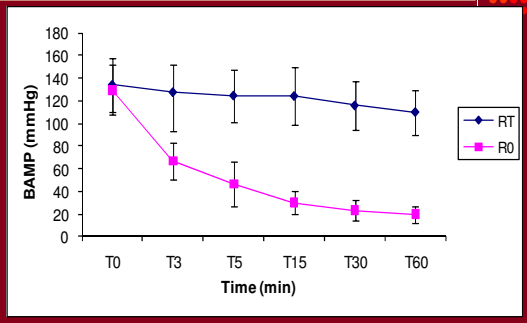

Scan J Immunol, 2003

## Histamine release during anaphylactic shock



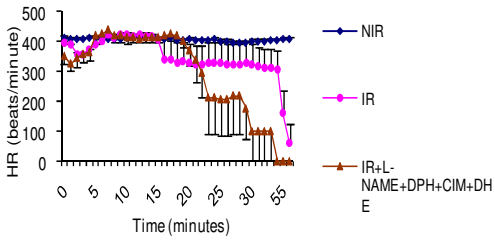

Shock, 2003

## Anaphylactic Shock



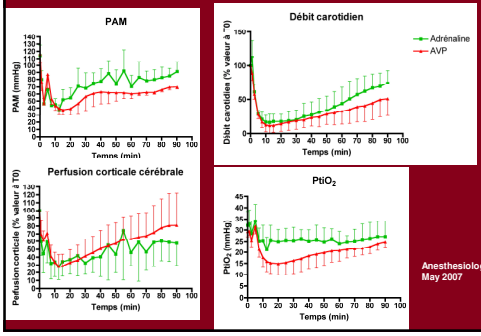

Shock, 2003

## Effect of NO Synthase, Histamine and Serotonine Inhibition Pathways




Shock, 2003

## New treatments of Anaphylactic Shock Adrenaline or vasopressin?




Anesthesiology, V 106, No 5, May 2007

## Definition

- **2nd symposium on definition and management of anaphylaxis:**

**« Severe allergic reaction with rapid onset and risk of death. »**

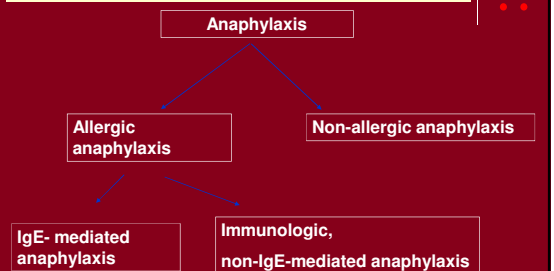
*(Sampson HA et al., JACI, 2006)*

- **World Allergy Organisation:**

**« Anaphylaxis is a severe life-threatening generalized or systemic hypersensitivity reaction. »**

*(Johansson SGO et al., JACI, 2004)*

## REVISED NOMENCLATURE FOR ANAPHYLAXIS




Johansson SGO et al JACI 2004;113:832-6

## INCIDENCE and PREVALENCE

- Indicators:
  - prevalence of all suspected allergic reaction with medical assistance
  - prevalence of severe reactions
  - prevalence of severe anaphylaxis complicated by death
- Results from different ways: registres, allergy network, hospitals, ED, Schools

## Prevalence in Emergency Departments

- Gaeta, 2007-Ann Allergy
  - 12 millions allergic reactions over 12 years (1993 à 2004) in US
  - 1% of all ED visits
  - 1 million per year

  **12,400 anaphylaxis per year in ED**

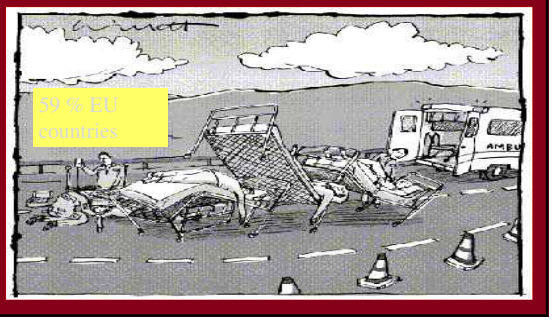
## Pre hospital setting

Ken, 2004-J Emerg Med : 10 US states

- no standardization of anaphylaxis definition
- 2.8 millions calls to the regulation centre=0.34 to 0.82% for allergy/anaphylaxis
- Adrenaline=1/10
- Mortality=0 to 0.94%

## Paramedics: American System


## Pre Hospital System Franco-German Model




## Mortality

- Review: **4 for 20,381 cases of anaphylaxis** cared in ED=**2 for 10,000**
- Moneret-Vautrin, 2005-Allergy
  0.65 to 2%=**1 to 3 for 1 million in Europe**
- Neugut, 2001-Arch Int Med : **20 pour 1 million in US**

## Mortality

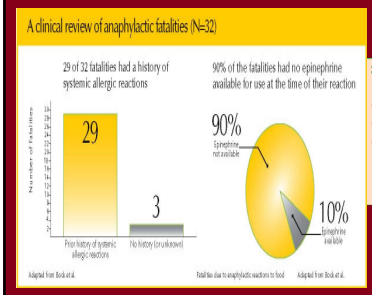
**Risk Factors:**

- Delayed adrenalin administration
- Beta blokers, convertase enzyme antagonists
- Asthma, co-morbidity
- Allergen introduced IV

**90% of died patients** had dyspnea before then cardiac arrest

**Drug allergy**=Shock is the main symptom

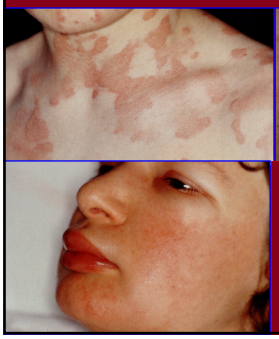
## Anaphylaxis and Food Allergy

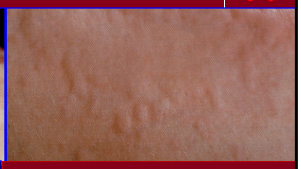



32 deaths in patients with age between 2 to 32 ans
- - peannut >90% of reations
- - history of asthma
- - majority didn't receive epinephrine

Bock SA et al. J Allergy Clin Immunol 2001;107:191-3

## Clinical Signs







Shock

Myocardial infarction
Cardiac arrest

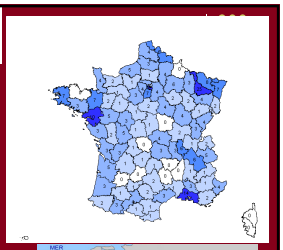
Cardiac anaphylaxis

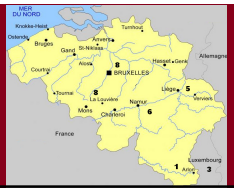
## French Allergy Vigilance Network

406 members ( 15 12 2007)

| | |
|---|---|
| Allergists | 231 |
| All and pediatricians | 59 |
| All and pulmonologists | 54 |
| All and internists | 14 |
| All et dermatologists | 15 |
| All et biologists | 16 |
| All et anesthesiologits | 2 |
| Others | 15 |

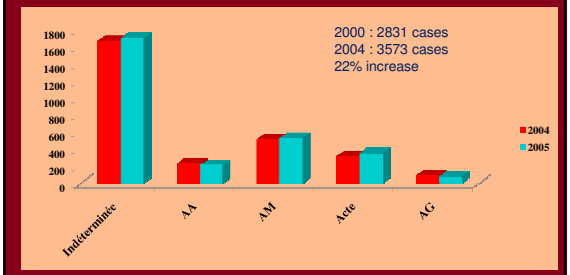
Dom Tom : Martinique(3), Guadeloupe(1), La Réunion(1), Nouvelle Calédonie(1)
Pays étrangers : Belgique(29), Luxembourg(3), Algérie(5), Italie(5), Maroc(4), UK(4)
Argentine(3), Chili(3), Pologne(3), Espagne(1), Suisse(1), Tunisie(1), USA(1), Grèce(1)
Hollande 1






Clin Exp Allergy, 2010

## French Allergy Vigilance Network




Clin Exp Allergy, 2010

## Allergy Network Clinical Aspects

- Child: 34%  Adults: 66%
- ED visit: 80.5%
- Adrenaline administration: 44.5%
- Hospitalization: 59.3%

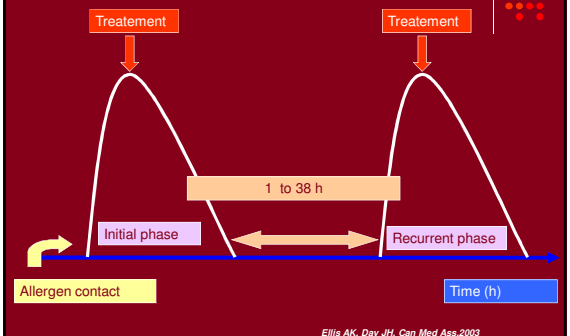
*Moneret-Vautrin et al Rev Méd Int 2006;120:S70-72*

## Allergy Network Clinical Aspects

- **Anaphylactic Shock: 47.6%**
- Severe systemic reactions: 36.7%
- Laryngeal Angio-Edema: 12.4%
- Severe asthma: 4.4%

*Moneret-Vautrin et al Rev Méd Int 2006;120:S70-72*

## Anaphylaxis: Biphasic Reaction




*Ellis AK, Day JH, Can Med Ass,2003*

## Meta-analysis

**1995 to 2001 : 5**

1- Schwartz, 1995-Allergy Proc : US
2- Klein, 1995-JACI US
3- Stewart, 1995-Q J Med UK
4- Pastorello, 2001-J Chrom Biomed Sc Appl Italy
5- Brown, 2001-JACI Australia

**2003 to 2008 : 12**

6- **Bellou**, 2003-Emerg Med J, France
7- Brown, 2004-JACI, Australia
8- Clarck, 2004-JACI, USA
9- Clarck, 2005-JACI, USA
10- Haymore, 2005-JACI, USA
11- De Villiers Smit, 2005-J Emerg Med Hong Kong
12- Luke, 2006-Ann Emerg Med, USA
13- Braganza, 2006-Arch Dis Child Australia
14- Gaeta, 2007-Ann Allergy, USA
15- Melville N, 2008-Emerg Med J, UK
16- De Silva IL, 2008-Allergy, Australia
17- Ross MP, 2008-JACI, USA

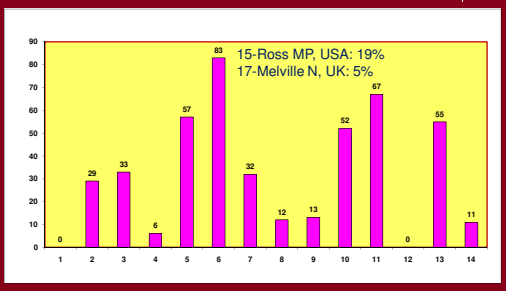
Eur J Emerg Med, 2010

## Type of Allergen

- Food : **33%**
- Hymenoptera Venom : **28%**
- Drugs : **26%**

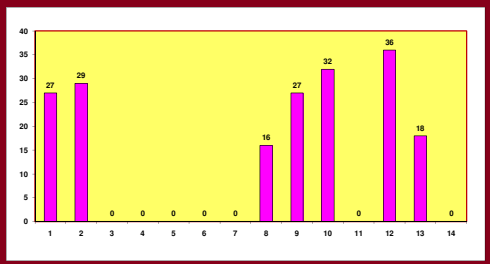
Bellou A: Eur J Emerg Med, 2010

## Adrenaline Administration in ED



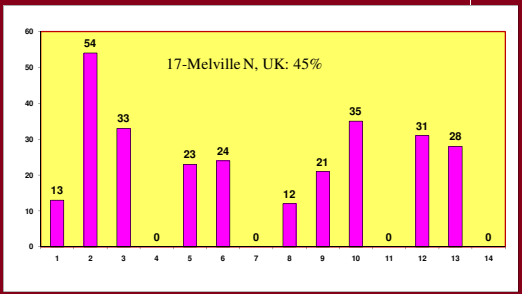

Bellou A: Eur J Emerg Med, 2010

## Adrenaline Self-injected



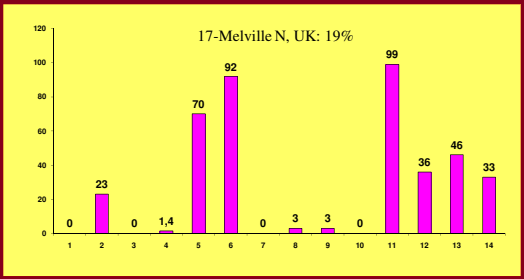

Bellou A: Eur J Emerg Med, 2010

## Allergist Follow-up




Bellou A: Eur J Emerg Med, 2010

## Hospitalisation after ED Care




Bellou A: Eur J Emerg Med, 2010

## Summary

- 75 to 85% of anaphylaxis are cared in EDs +++
- 4 guideline recommendations not respected:
  (1) **adrenaline at the acute phase,**
  (2) **prescription of self-injected adrenaline,**
  (3) **education of patient,**
  (4) **follow-up by allergist**

## GUIDELINES

- **Anaphylaxis network symposium:**

J Allergy Clin Immunol 2006 ;117 : 391-7

**Definition : severe allergic reaction with sudden onset and risk of death**

## Diagnostic of Anaphylaxis

**Criteria 1 :** skin lesions and/or mucosa lesions (urticaria, itching or erythema, lips oedema or tongue-uvula edema). With one or mors following signs :

- Respiratory troubles (dyspnea, bronchospasm, stridor, decreased of peak flow, hypoxia)
- Systolic BP<90 mmHg) ou organ dysfunction (hypotonia, syncope, incontinence)

## Diagnostic of Anaphylaxis

**Criteria 2 :** 2 or more signs after exposition to a ***probable allergen***:

- skin lesions and/or mucosa lesions (urticaria, itching or erythema, lips oedema or tongue-uvula edema). With one or mors following signs :
- Respiratory troubles (dyspnea, bronchospasm, stridor, decreased of peak flow, hypoxia)
- Systolic BP<90 mmHg) ou organ dysfunction (hypotonia, syncope, incontinence)
- Persistant gastrointestinal troubles (abdominal pain, vomiting)

## Diagnostic of Anaphylaxis

**Criteria 3:** Decrease of SBP< 90mmHg or more than 30% compared to basal in adults* after exposition to ***known allergen***.

*In child decrease of SBP is defined as: SBP < 70 mmHg from 1 month to 1 year, below (70 mmHg + [2 x age]) from 1 to 10 years, <90mmHg from 11 to 17 years.

## Guidelines

- **Anaphylaxis network symposium :**

J Allergy Clin Immunol 2006 ;117 : 391-7

Self-injected Adrenaline: cardiovascular or respiratory signs and know allergen

Information of patient

Allergy follow-up after ED visit

Monitoring in ED: 8 to 24 h, hospitalisation for severe or recurrent anaphylaxis, asthmatic patient

## Self-injected epinephrine

## Self-injected epinephrine

## Self-injected epinephrine

## Guidelines for ED Treatement

- Suspicion of severe anaphylaxis
- ABC
- Diagnostic (definition)
- 1e line : Adrenaline + Fluid resuscitation: crystalloïds or saline 0.9%, adult 500 ml to1000 ml ( up to 4000ml), children 20ml/Kg

Jasmeet S. Resuscitation 2008;77:157-169.

## Adrenaline

- **Adrenaline IM: dilution 1/1000**
- Adult : **500 microgrammes (0,5ml)**
- Child > 12 years: **500 microgrammes (0,5ml)**
- Child 6 to 12 years: **300 microgrammes (0,3ml)**
- Child < 6 years: **150 microgrammes (0,15ml)**

Jasmeet S. Resuscitation 2008;77:157-169.

## Adrenaline

- **IV: dilution 1/10000** (10 ml with 100 microgrammes/ml adrénaline), routinely used by EPs:
  - Adult: bolus of **50 microgrammes (0,5ml)**
  - Child: bolus of 1 microgramme/Kg
  - If repeated administration=perfusion by pump (1 to 4 microgrammes/min).

Jasmeet S. Resuscitation 2008;77:157-169.

## Second line treatment

- **Histamine antagonists**

Dexchlorpheniramine=against itching

- **Corticosteroids**

Hydrocortisone-Methylprednisolone=prevent recurrent anaphylaxis

Jasmeet S. Resuscitation 2008;77:157-169.

## Guidelines for ED Treatement

- **Specific situations**

Glucagon : 1-2 mg every 5 min, resistance to adrenaline, patient treaed by β blokers

Cradiac arrest :

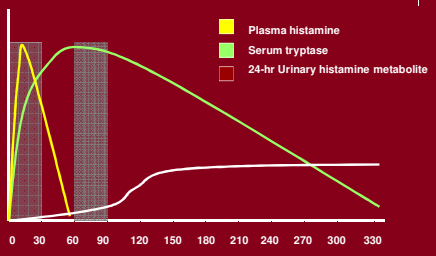
follow current guidelines
fluid resuscitation=4 to 8l
adrenaline : 1 to 3 mg IV (3min), 3 to 5 mg (3min), 4 to 10 microg/min pump perfusion

## Positive Diagnosis in ED

- **Medical history to identify allergen**
- **Tryptase**
  - Specific for mast cells degranulation, confirm anaphylactic reaction
  - Still increased at 6th hour

Lieberman PL et al, J Allergy Clin Immunol 2005;115:S483-523

## Biologic tests in anaphylaxis Kinetic




**T1** = after emergency treatment start, **T2** = 1 to 2 h after T1 et **T3** at 24 h in the ward. Put serum at -20°C.

## CONCLUSION

- **EPs : critical role=first line**
- **Improve knowledge in Allergy**
- **Use Adrenaline even without hypotension**
- **Collaboration with allergist is essential**
- **Developp research in anaphylaxis (if interested we recruit master and PhD, abdel.bellou@voila.fr)**