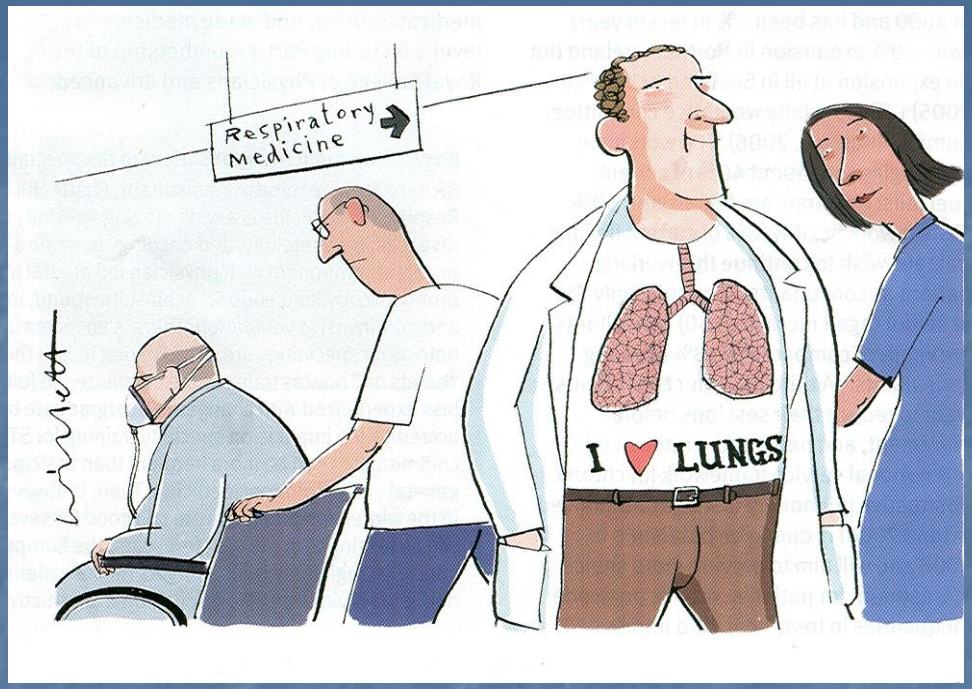
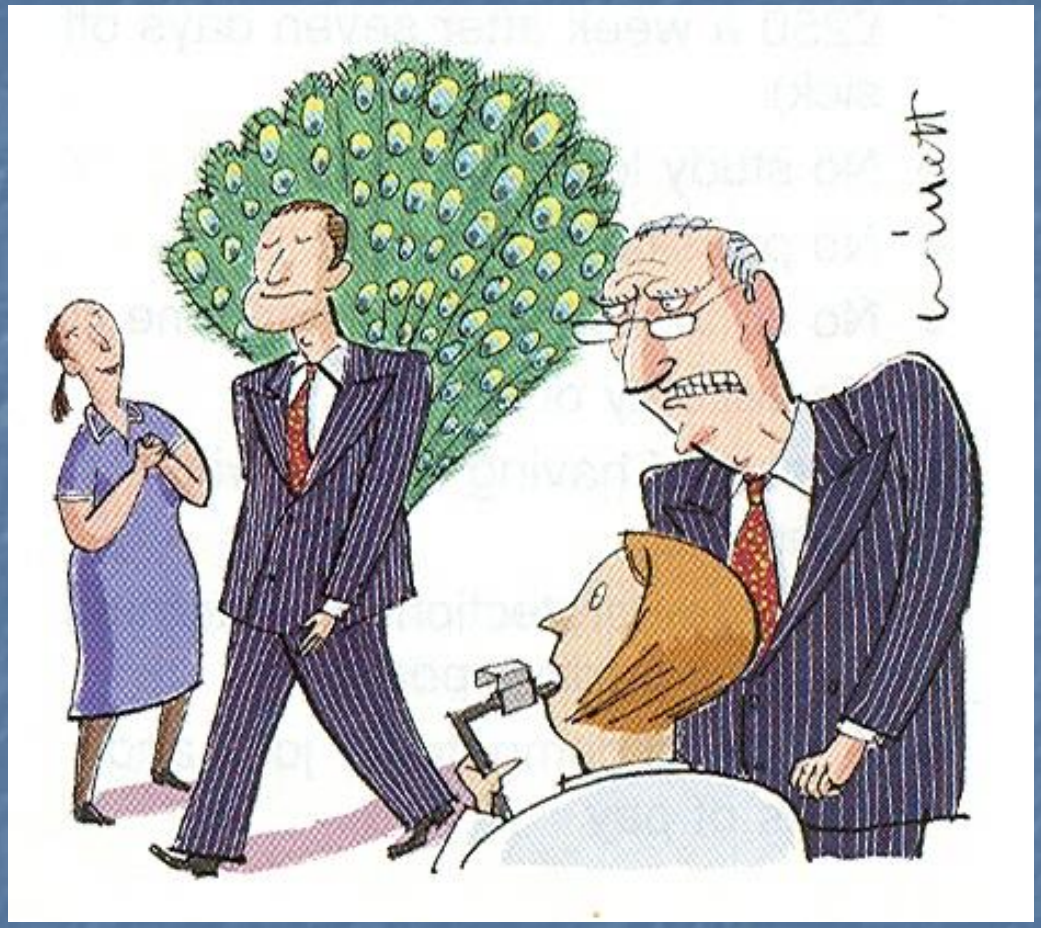


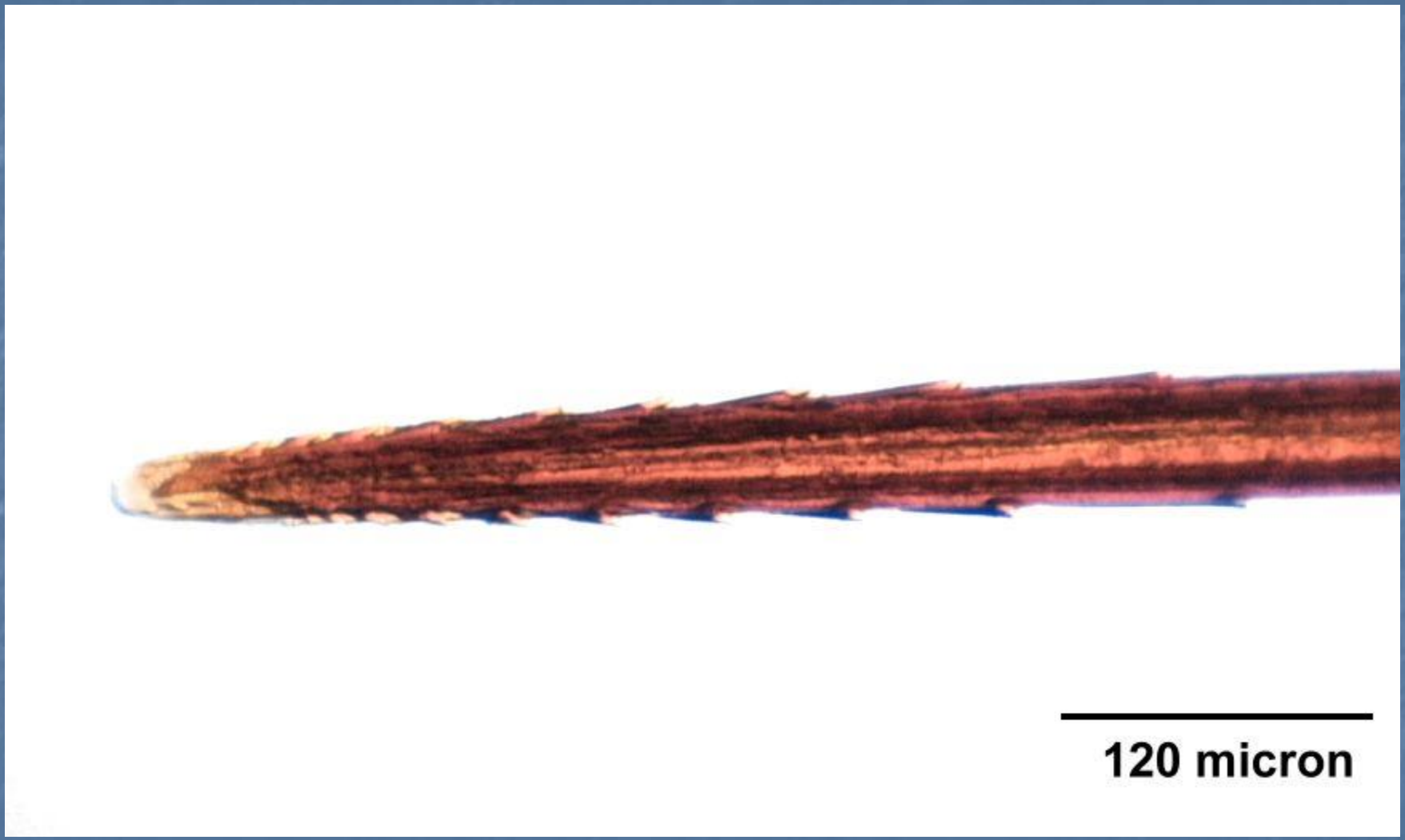
Dr Stephen Kelly
Consultant Respiratory Physician
Bees and allergy

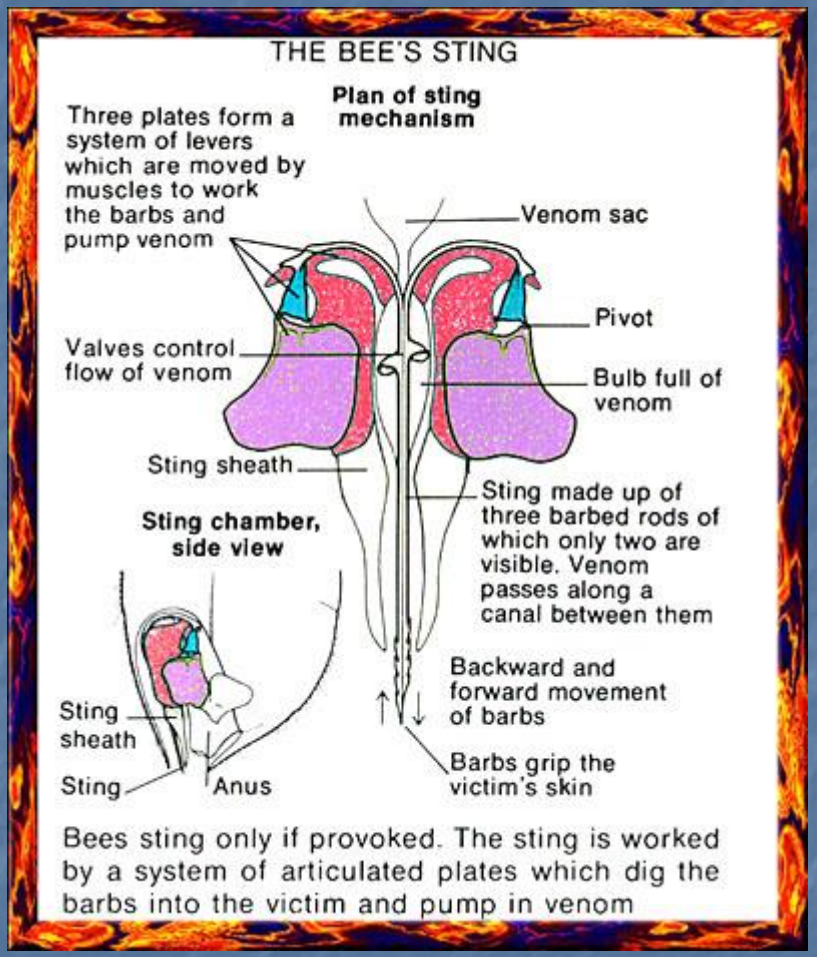


Bee Stings

- partial misconception that worker can sting only once
- sting is barbed so that it lodges in the victim's skin, tearing loose from the bee's abdomen and leading to its death in minutes
- This only happens if the victim is a mammal (or bird)

- bee's sting evolved originally for inter-bee combat
- the barbs evolved later as an anti-mammal defense
- barbed sting can still penetrate the chitinous plates of another bee's exoskeleton and retract safely
- Honey bees are the only Hymenoptera with a strongly barbed sting, though yellow jackets and some other wasps have small barbs


120 micron


THE BEE'S STING
Plan of sting mechanism
Three plates form a system of levers which are moved by muscles to work the barbs and pump venom
Venom sac
Pivot
Valves control flow of venom
Bulb full of venom
Sting sheath
Sting made up of three barbed rods of which only two are visible. Venom passes along a canal between them
Sting chamber, side view
Backward and forward movement of barbs
Sting sheath
Sting
Anus
Barbs grip the victim's skin
Bees sting only if provoked. The sting is worked by a system of articulated plates which dig the barbs into the victim and pump in venom

- Injects apitoxin into victim

- releases alarm pheromones
  - alarm pheromones near a hive or swarm attracts other bees to the location, where they will exhibit defensive behavior until there is no longer a threat, typically because the victim has either fled or been killed

- pheromones do not dissipate or wash off quickly
- if target enters water, bees will resume their attack as soon as it leave
- drones no sting
- queen bee has a smooth sting and can, if need be, sting skin-bearing creatures multiple times
- Queen only uses it for dispatching rival queens
- Queen breeders who handle multiple queens and have the queen odor on their hands are sometimes stung

- main component of bee venom responsible for pain in vertebrates is the toxin melittin

- histamine and other biogenic amines also contribute to pain and itching

- apitherapy
  - bee venom has been used to treat arthritis and other painful conditions

Management of bee stings

- 1st step is removal of the sting itself.
- removed as fast as possible without regard to method
  - studies have shown the amount of venom delivered does not differ if the sting is pinched or scraped off and even a delay of a few seconds leads to more venom being injected
- Once the sting is removed, pain and swelling should be reduced with a cold compress

Many traditional remedies have been suggested for bee stings including:

- Damp pastes of tobacco
- Salt
- Baking soda
- Meat tenderizer
- Toothpaste
- Clay
- Garlic
- Urine
- Onions
- Aspirin
- Application of copper coins

- Bee venom is acidic these and such methods are recommended to neutralize the venom

- neutralizing is unlikely to be effective as the venom is injected under the skin and deep into the tissues, where a topically applied alkali is unable to reach

- amount of venom injected is typically very small (between 5-50 mcg) so placing large amounts of alkali near the sting site is unlikely to produce a perfectly neutral pH to stop the pain

- No scientific evidence of any of these methods being useful

- randomized trial of aspirin paste and topical ice packs showed that aspirin was not effective in reducing the duration of swelling or pain in bee and wasp stings, and significantly increased the duration of redness
  - ice alone is better treatment for bee and wasp stings than aspirin
- sting may be painful for a few hour
- Swelling and itching may persist for a week

- area should not be scratched as it will increase the itching and swelling

- If a reaction persists for over a week or covers an area greater than 3 or 4 inches, medical attention should be sought

- venom differs between species

- in humans it is generally the allergic element of the venom falls into two categories:
  - Bees
  - wasp/hornet venom

- common for individuals to be allergic to one venom and not the other

- Similarly if you are allergic to a single type of wasp, then there is a high possibility that you will be allergic to others in the hymenoptera family

Bee Venom

- Enzymes
- Peptides
- Mixture small organic molecules

- Most important constituents to which sensitisation can occur are:
  - Phospholipase A_2
  - hyaluronidase

Bee Venom

- Peptides cause mast cell degranulation
- Releases histamine with subsequent inflammatory response
- Apamin only true neurotoxin in venom

Problems of bee stings

- They hurt!
- Localised issues
- Massive attacks
- Anaphylaxis

- Most people can tolerate 15-25 stings without requiring special medical treatment
- Pain, redness and swelling are normal at a sting site and this does not constitute an allergic reaction
- If you receive > 15-25 stings should seek medical supervision for possible delayed systemic complications

Localised problems

- Stings on the eye
  - Optic neuritis with:
    - severe pain
    - Loss of vision
    - Optic disc swelling

Mass attacks

- Massive bee en-venomation can produce both immediate and delayed toxic reaction
- Signs and symptoms of immediate toxic reaction are:
  - Fatigue
  - Nausea
  - Vomiting
  - Haemolysis
  - kidney failure
  - disseminated intravascular coagulation

- Delayed toxic reaction
  - Initially asymptomatic after a massive bee envenomation, with normal initial lab results
  - But later demonstrates evidence of
    - Haemolysis
    - Coagulopathy
    - Thrombocytopenia
    - Rhabdomyolysis
    - liver dysfunction
    - disseminated intravascular coagulation

- Due to such delayed toxic reactions guidelines in one US hospital:

- recommend 24 hour hospital observation for paediatric patients, older patients, and patients with underlying medical problems who are asymptomatic or who are experiencing only pain after an envenomation of 50 or more stings

- 6 hours for other subjects

Treatment

- Supportive with:
  - Intravenous fluids
  - blood products
  - Dialysis
  - etc

- In mass attack can be direct neurotoxic problems:
- Guillain-Barre syndrome
  - Ascending muscle weakness
  - Paralysis
- Can be associated with seizures
- CVA/TIA features

African Bees/'killer bees

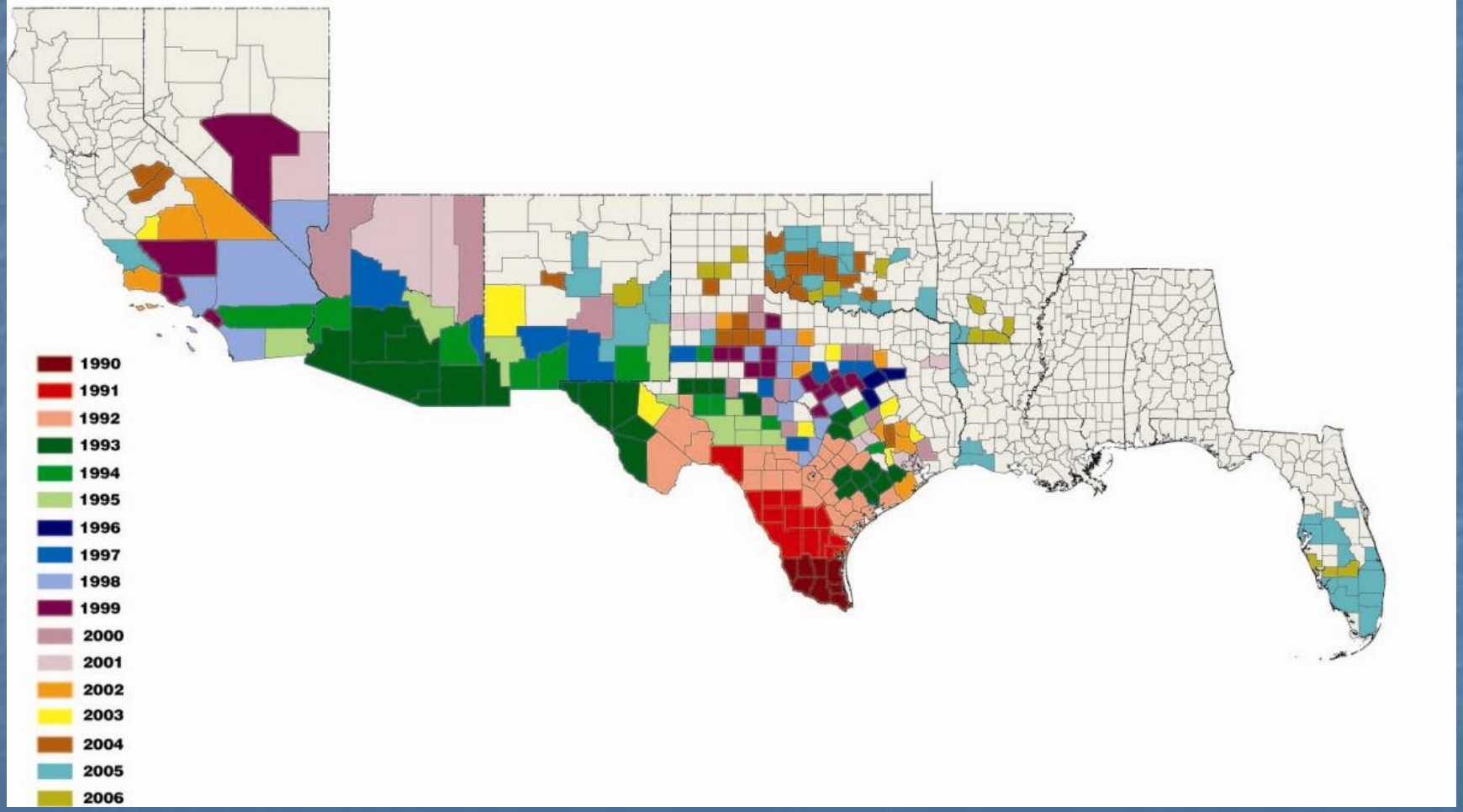
- Accidental introduction of native African bee *Apis mellifera scutellata* in Brazil in 1957
- Displaced and hybridised with long established European *A m mellifera and A m ligustica*
- More aggressive
- Better adapted to warm climates so successful and rapid spread


1994
United States
Texas
Mexico
1993
1988
1990
1995
1997
1994
1991
1990
1992
Venezuela
Guyana
Suriname
French Guiana
Colombia
Ecuador
Peru
Brazil
Bolivia
1967
Paraguay
Chile
Argentina
Uruguay
1977

Spread of Africanized honey bees by year, by county

Updated January 2007

First found in southern Texas in 1990, Africanized honey bees are now found in much of the South.



- Attack more readily
- Attack in greater numbers
- Can be >1000 on an individual
- Approx 50 can cause systemic envenoming
- >500 to cause death by direct toxicity
- By 1985 estimated to have caused 700-1,000 deaths
- Approx 60 per year in Mexico

- Inject less venom than european bees
  - Average 94mcg vs 147mcg

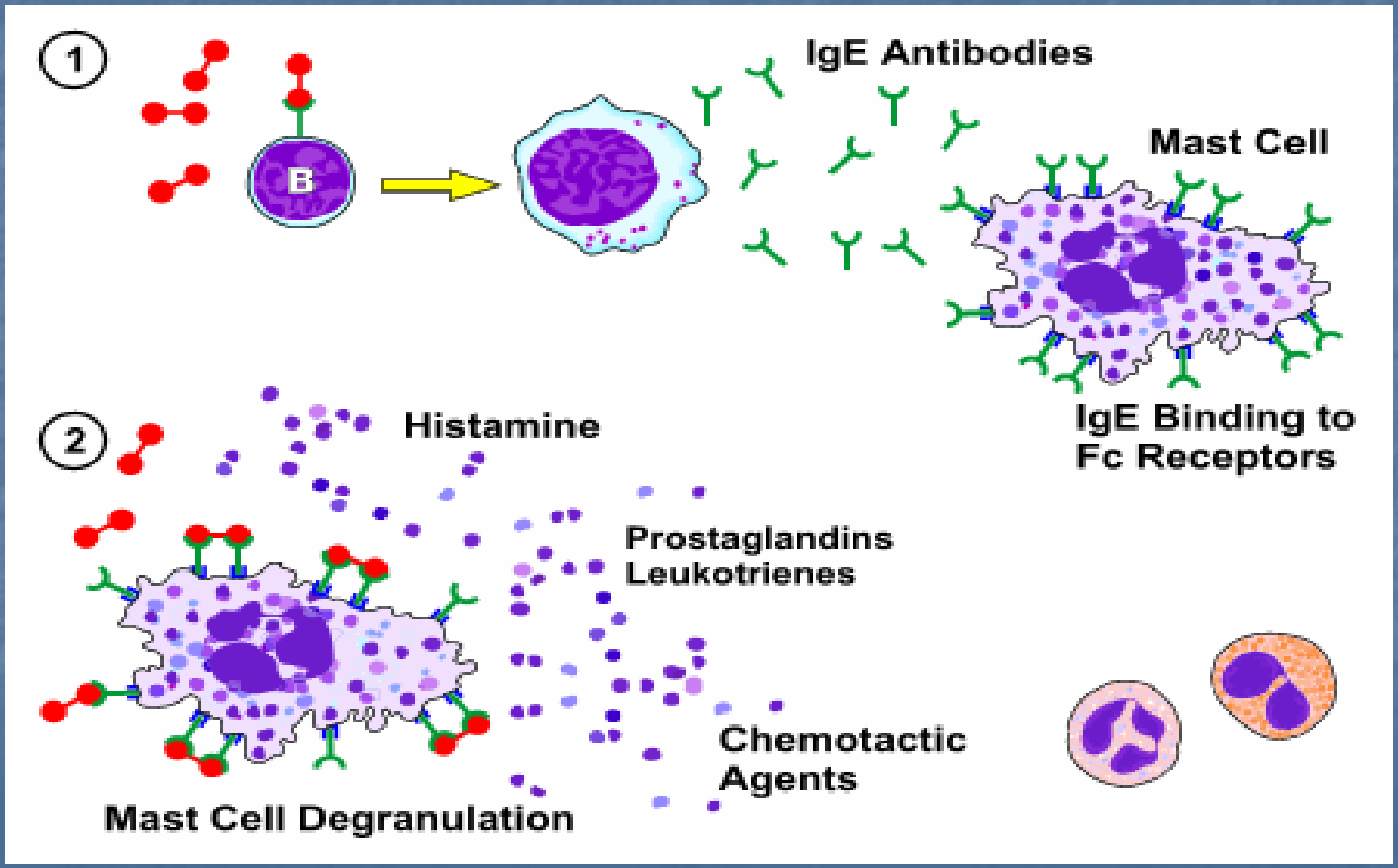
- Death from nonspecific membrane effects
  - Haemolysis
  - Coagulopathy
  - Thrombocytopenia
  - Rhabdomyolysis
  - liver dysfunction
  - disseminated intravascular coagulation

Trait	Africanized	European
open, exposed nests	common	rare
location of nests	variable; any kind of cavity including in-ground animal nests, which increases likelihood of human contact	prefer larger cavities, bee hives, hollow trees, hollow walls; rarely in ground
		
tendency to abandon nest	frequent	rare
swarming rate	higher	lower
stinging behavior	intense; can defend nest at distances of up to 100 yards	moderate to mild; defend nest from 1-20 yards
body size	about 10-20% smaller than European	larger
development time for worker bee	19-20 days	21 days
honey production	acceptable once beekeepers adapt	industry standard
pollination	effective pollinators but risky to farm laborers	industry standard
tolerance of mechanized handling	acceptable if beekeeper limits hives to one per stand or pallet; netting	industry standard

Allergy (Type 1)

- Allergy develops after repeated exposure to the causative allergen
- This sensitisation takes place on initial exposure and no adverse reaction appears to occur
- Tendency some families have to develop allergic sensitisation is termed "Atopy“

Type I - Immediate



- During sensitisation produce IgE
- On re-exposure get immediate reaction and late phase at about 6-24 hours
- Can be sensitised to an allergen and have positive allergy tests but not ever have an allergic reaction (Latent Allergy)
- Common Type I Allergic reations include
  - Asthma
  - Allergic Rhinitis or Hayfever
  - Atopic Eczema
  - Contact Dermatitis
  - Urticaria
  - Food Allergy
  - Wasp Venom Allergy
  - Drug allergy eg Penicillin

Type I

- IgE mediated in pre-exposed individuals
- Two phases: <30 minutes and 6-8 hours
- Examples
  - Penicillin allergy
  - Urticaria caused by drugs
- Treatment
  - Adrenaline
  - Corticosteroids
  - Antihistamine

Tests

- Skin Prick test
- Sp IgE level
- Flowcast

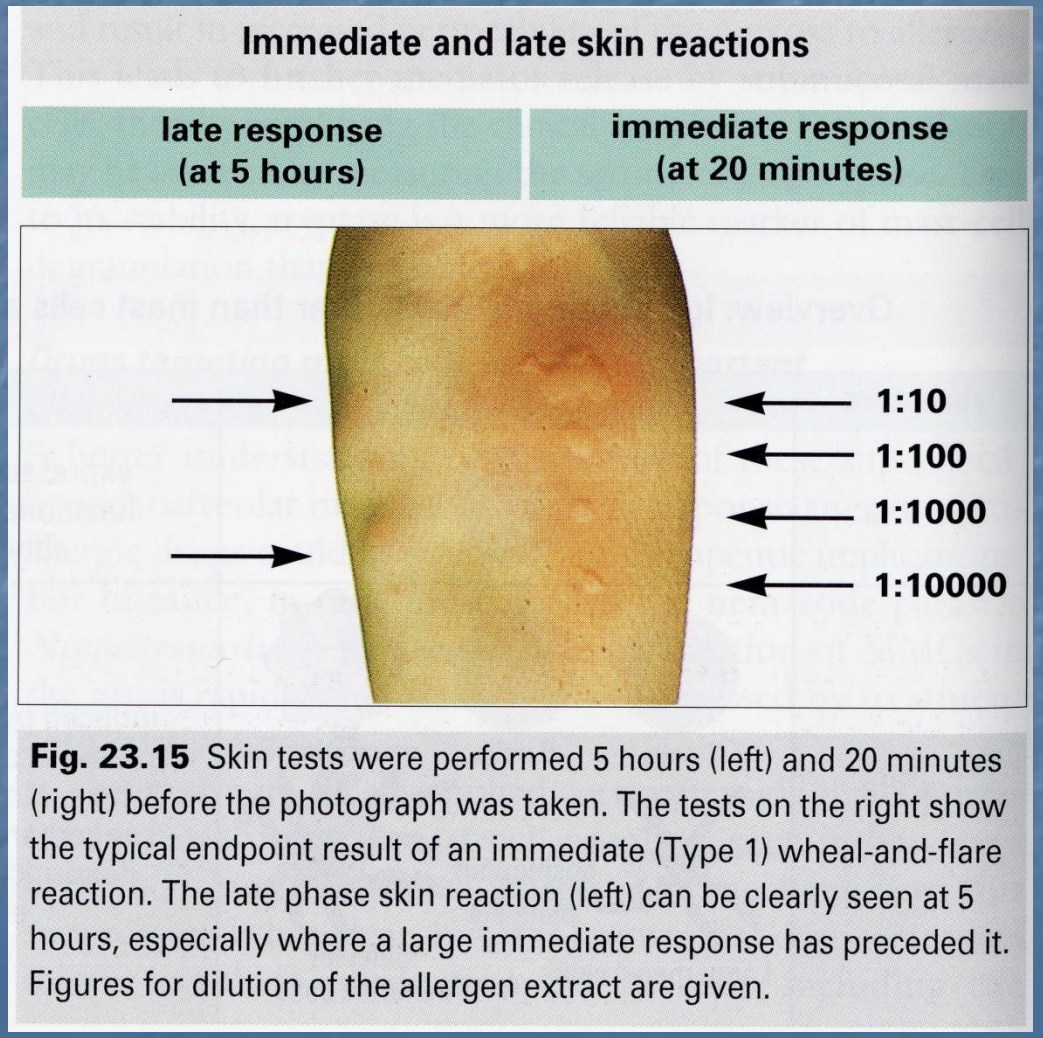
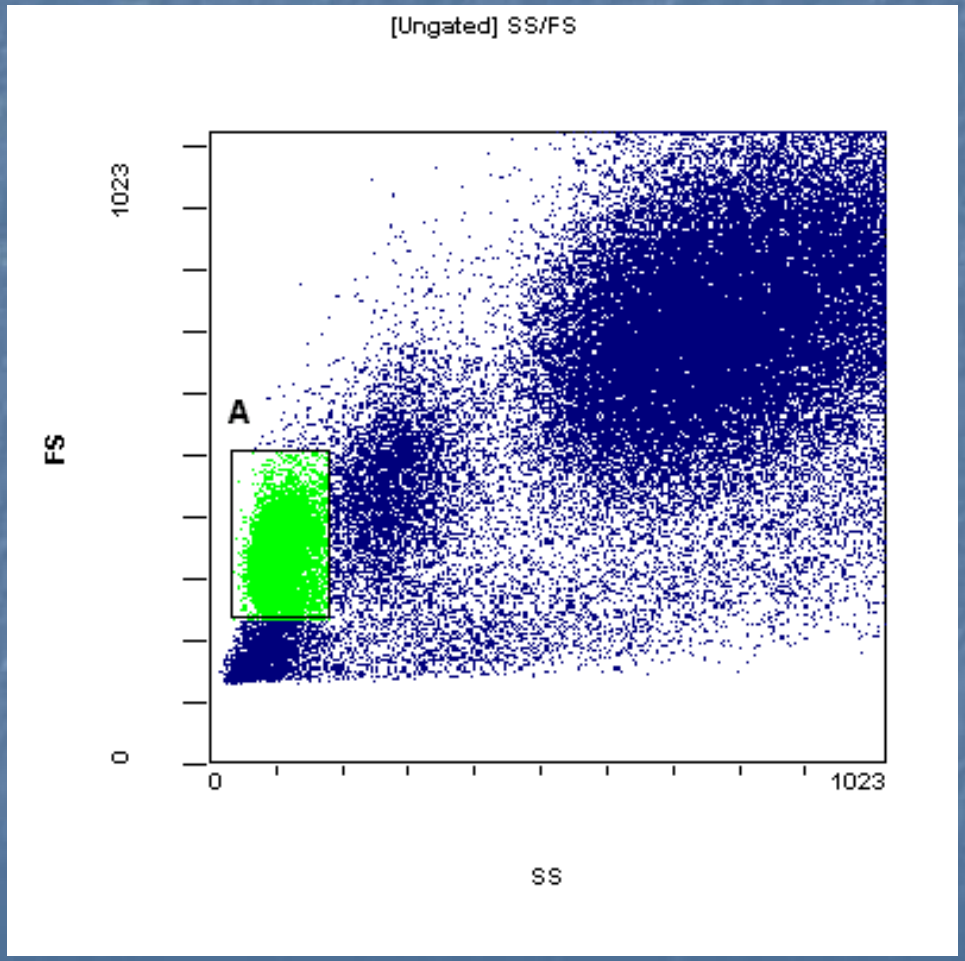
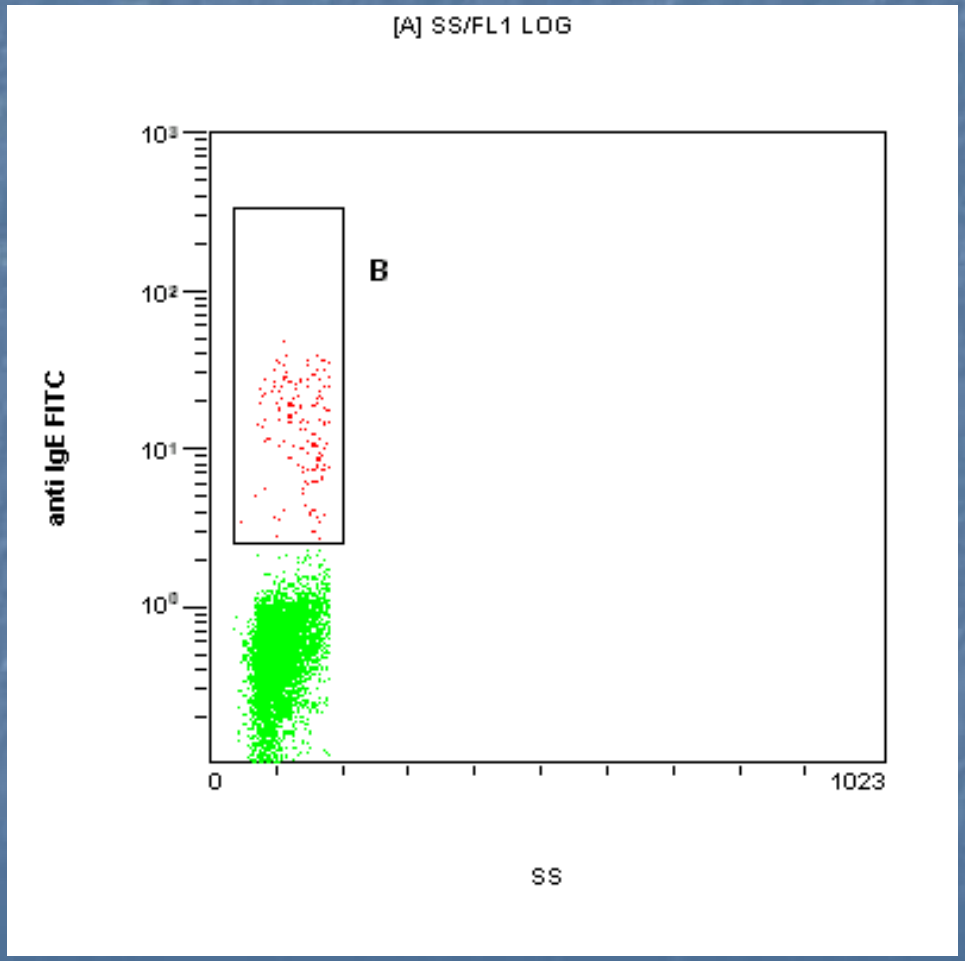


Fig. 23.15 Skin tests were performed 5 hours (left) and 20 minutes (right) before the photograph was taken. The tests on the right show the typical endpoint result of an immediate (Type 1) wheal-and-flare reaction. The late phase skin reaction (left) can be clearly seen at 5 hours, especially where a large immediate response has preceded it. Figures for dilution of the allergen extract are given.

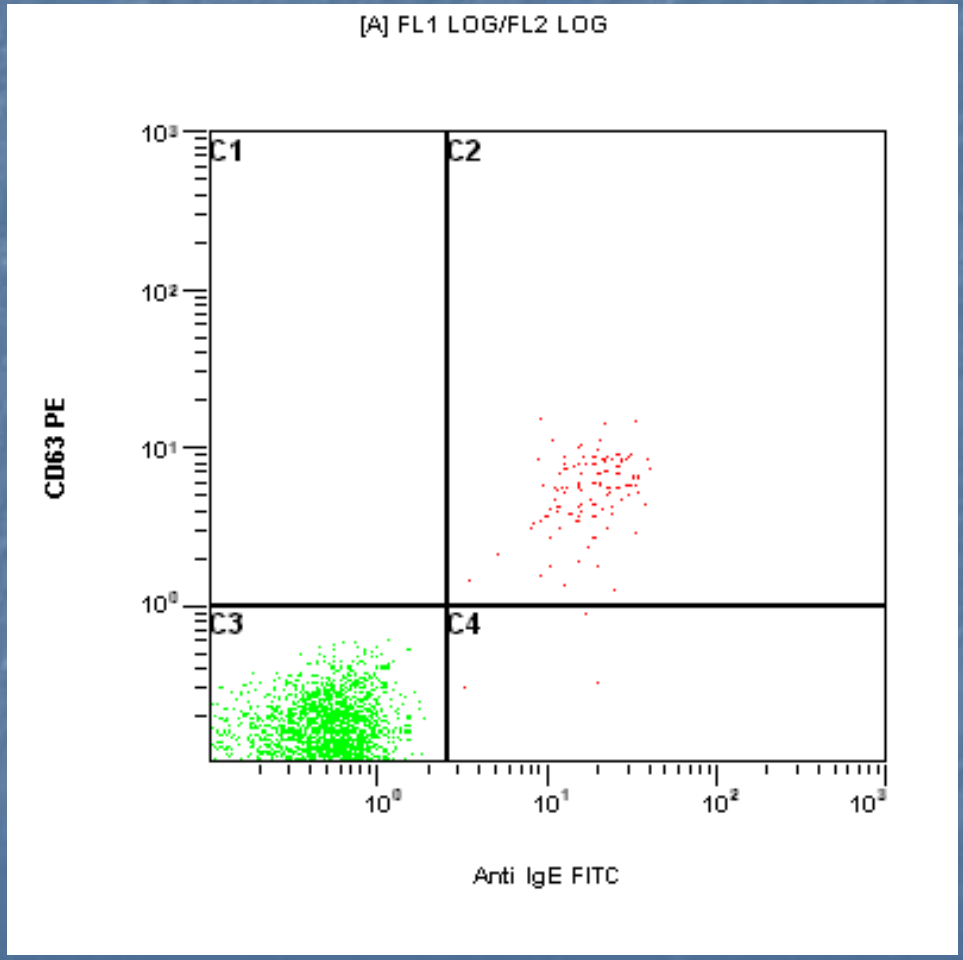
Buffy Coat Sample Lymphocyte gate A

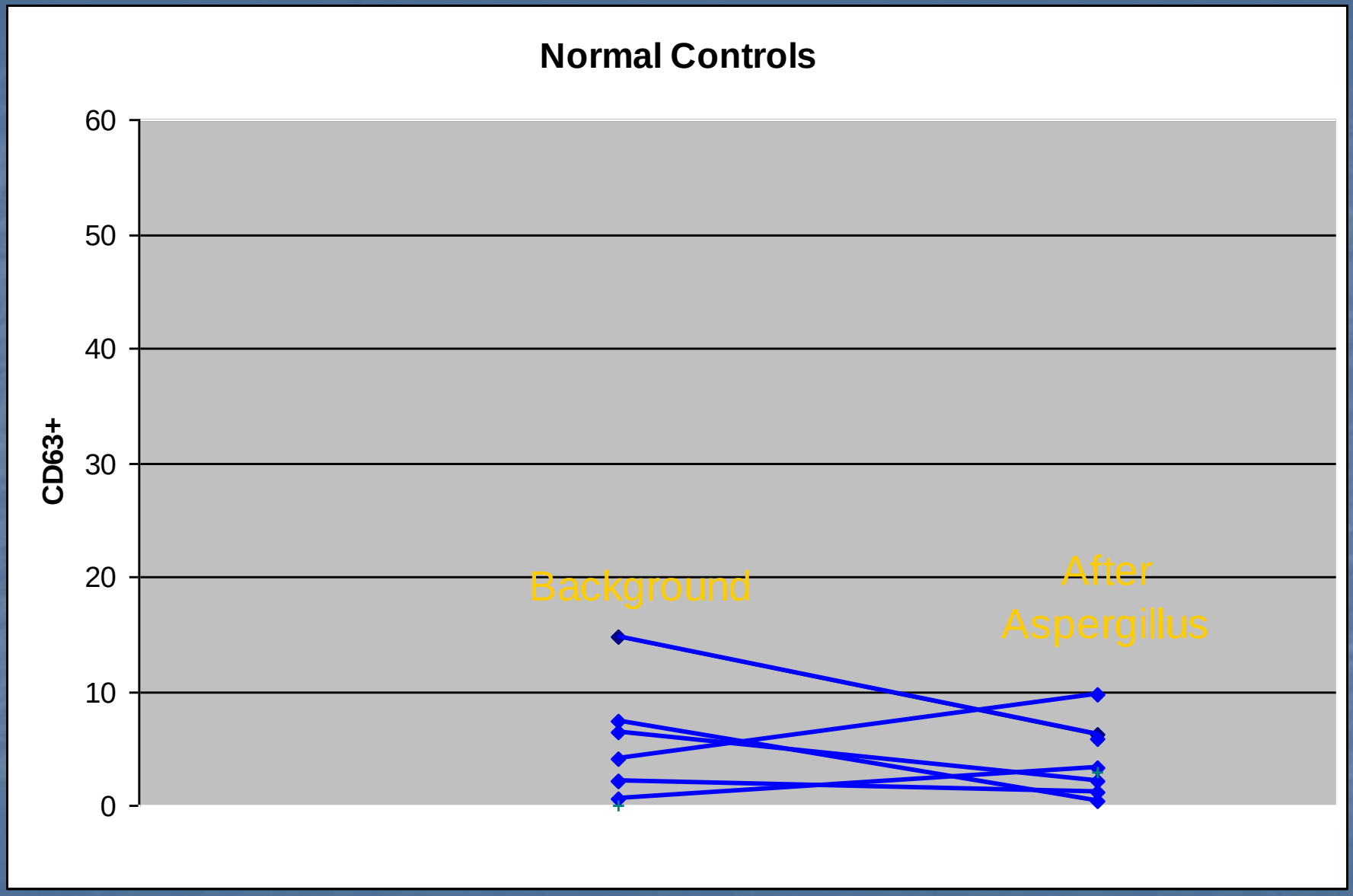


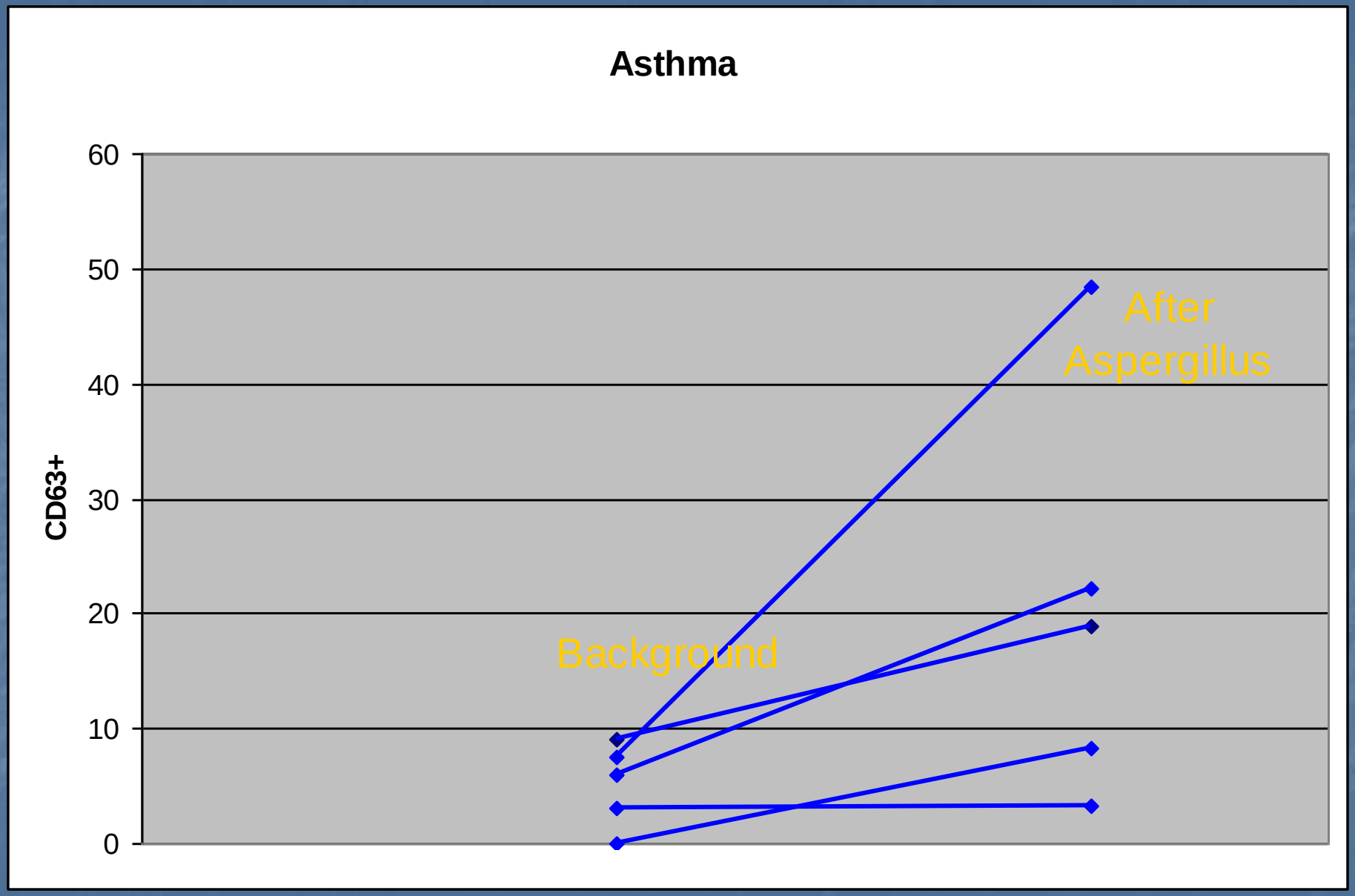
Basophil isolation from lymphocyte gate using Anti-IgE FITC



Basophil CD63 expression after *Aspergillus fumigatus* allergen exposure




Normal Controls
CD63+
60
50
40
30
20
10
0
Background
After Aspergillus


Asthma
CD63+
60
50
40
30
20
10
0
After Aspergillus
Background

Allergic breakthrough

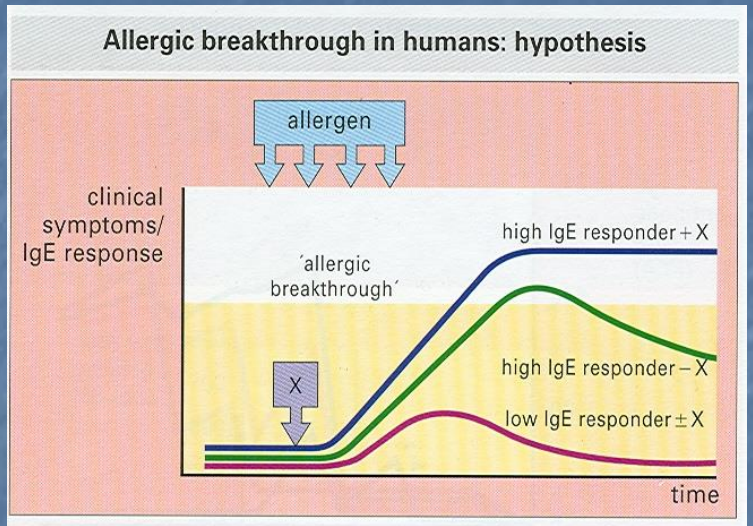


Fig. 23.27 On exposure to allergen an IgE response may develop transiently in low IgE responders before being controlled by suppressor T-cell activity and/or a change in the T_H1/T_H2 balance of the immune response. In high responders, the IgE response to allergen is much greater than in low responders, but the overt expression of clinical symptoms is only seen at the point of allergic breakthrough. This may depend on the presence of concomitant factors (X) such as viral infections of the upper respiratory tract, transient IgA deficiency or decreased suppressor T-cell activity, which augment IgE responses and the development of clinical symptoms. In the absence of factor X, the high responder subject may not show clinical symptoms after a short period of allergen exposure alone, but may be induced to express clinical symptoms of allergy by further exposure to allergen and factor X.

- Clinical symptoms when arbitrary level of immunological activity reached

Anaphylaxis

- Clinical syndrome:
  - Urticaria
  - Angioedema
  - Bronchconstriction
  - Hypotension
  - Death possible

IgE mediated

1 in 15,000-23,000 A+E attendances

164 deaths in UK between 1992-8

- Adrenaline
  - ↑ peripheral vascular resistance (α receptors)
    - Thus improves BP and coronary perfusion
  - + inotrope (β_1 receptors)
  - Bronchdilator (β_2 receptors)

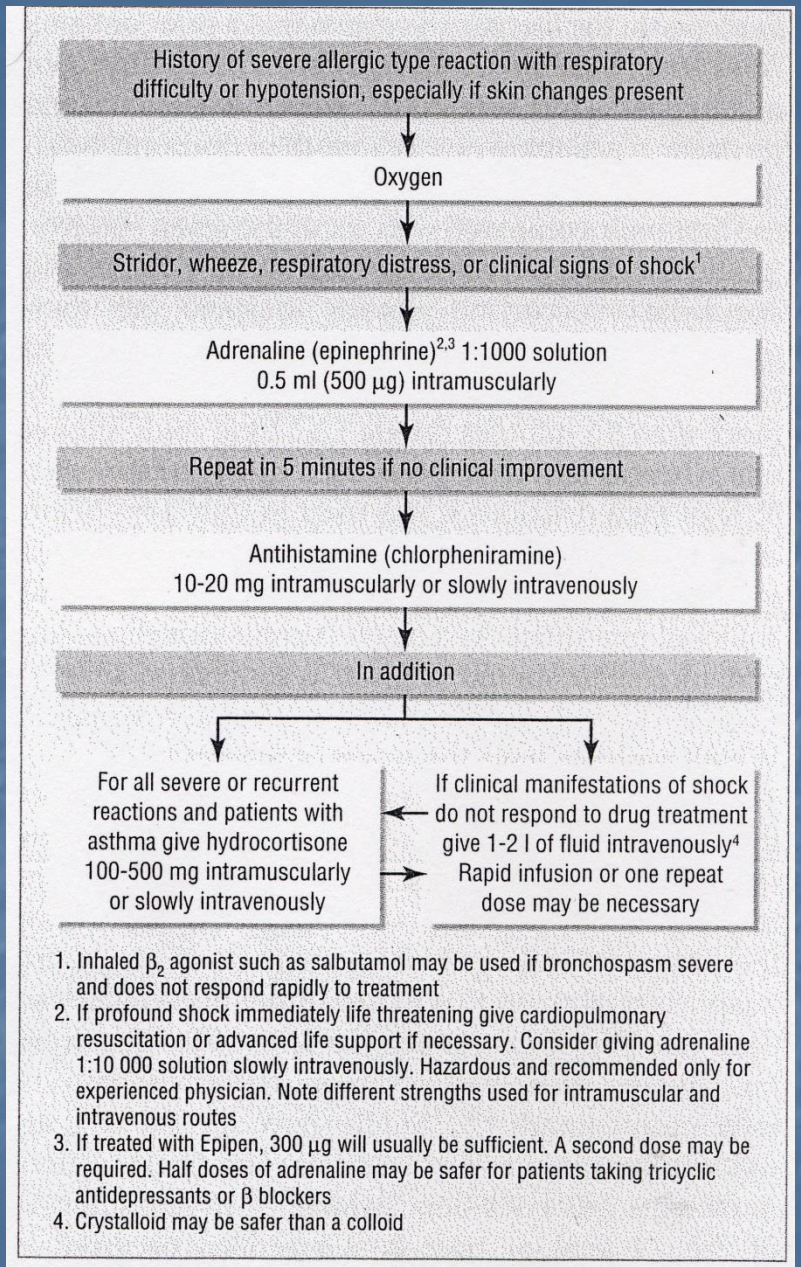
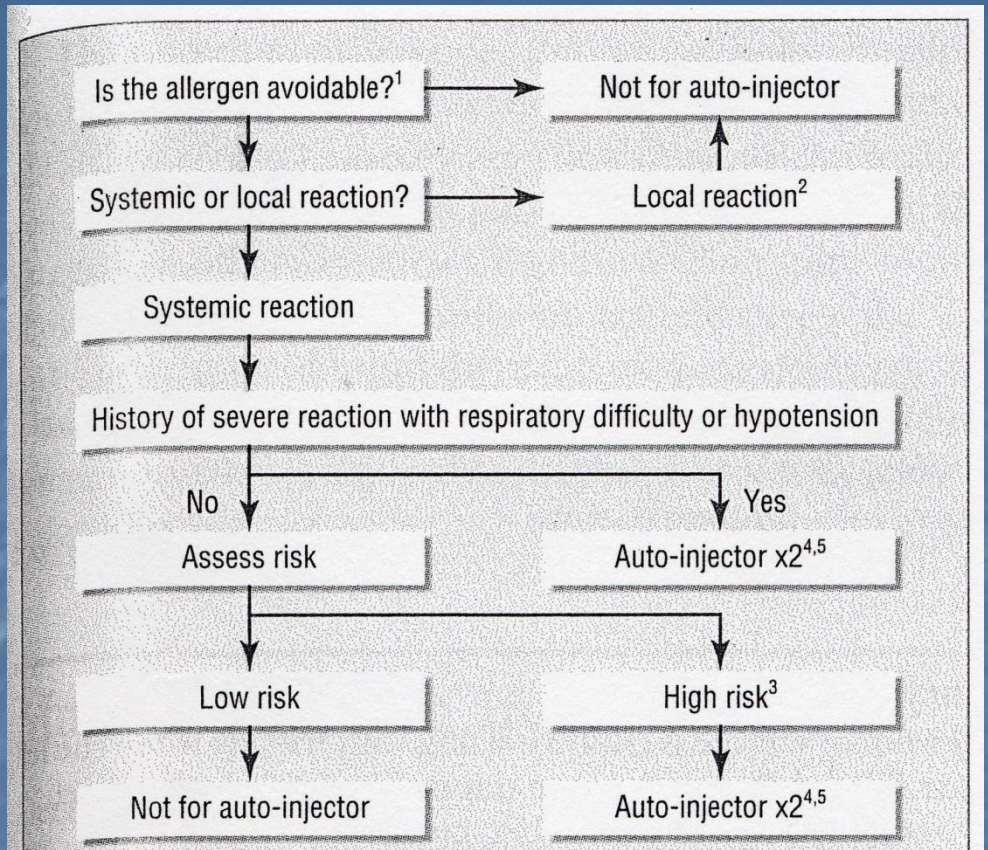


Fig 1 Algorithm for the treatment of anaphylaxis. Reproduced with permission of UK Resuscitation Council



1. No need for adrenaline (epinephrine) if allergen easily avoidable–for example, drug reaction
2. Excluding local involvement of the airway, including tongue swelling
3. Patients at high risk are those with asthma; reaction to trace allergen only, repeated exposure to allergen likely and lack of access to emergency medical care. Comorbidity may alter risk to benefit ratio
4. Patient (or carer) must be capable of understanding the indications for its use as well as physically able to use device
5. Consider adjustments to medication if taking β blockers, tricyclic antidepressants, or monoamine oxidase inhibitors

Fig 3 Algorithm for identifying patients who may benefit from an adrenaline auto-injector

β Tryptase

- Protein from mast cells
- In secretory granules
- > stability than histamine
- Can measure up to 2-4 hours after degranulation
  - Normal < 1ng/ml
  - Anaphylaxis >5ng/ml

Causes of Anaphylaxis reactions

I. IgE mediated
- A. **Native proteins (complete antigens)**
  1. **Foods**

     Fish, shellfish, crustaceans, eggs, milk, peanuts, nuts, fruits such as kiwifruit, and seeds (cottonseed, sesame, and psyllium) are the most common foods implicated.
  2. **Animal and Human Proteins**

     Stinging insects (hymenoptera, fire ants), biting insects (kissing bug or triatoma)
     Antilymphocyte globulin (ALG)
     Avian-based vaccine (measles, mumps, influenza, and yellow fever)
     Murine-derived monoclonal antibodies
     Seminal fluid
  3. **Hormones**

     Insulin, corticotropin (ACTH)
  4. **Enzymes**

     Streptokinase, chymopapain
  5. **Aeroallergens**

     Skin test or Immunotherapy for pollens, house dust mites, and molds
  6. **Others**

     Latex (gloves and other medical devices), protamine
- B. **Haptens (IgE-mediated reactions against the protein hapten conjugate)**
  1. **Antibiotics**

     Penicillin, cephalosporins, sulfonamides, and streptomycin
  2. **Disinfectants**

     Ethylene oxide
  3. **Smooth muscle relaxants such as succinylcholine**

II. **Non-IgE mediated**
- A. **Complement activation** and generation of anaphylotoxins (C3a, C4a, C5a)

  Human plasma and blood products, gamma globulin
- B. **Direct activation of mast cell or basophil** mediators

  Opiates, tubucurare, dextran, radiocontrast materials, fluorescein dye for angiography, and some chemotherapeutic agents.
- C. **Modulators of arachidonic acid metabolism**

  Nonsteroidal anti-inflammatory drugs such aspirin, ibuprofen, and indomethacin.

III. **Unknown Mechanism**
- A. **Sulfites**

  Food additives
- B. **Steroids**

  Progesterone and hydrocortisone
- C. **Physical triggers**

  (Exercise-induced anaphylaxis, food-dependent exercise-induced anaphylaxis, systemic cold-induced urticaria, and systemic heat-induced urticaria)
- D. **Systemic mastocytosis**
- E. **Idiopathic anaphylaxis**

Food allergy

- Minefield
- 15% of the population report having had adverse food reactions
- true prevalence of food allergy 1- 4% (6% children)
- general public perceive that food-related allergy is under-diagnosed
- doctors feel that it is over-diagnosed

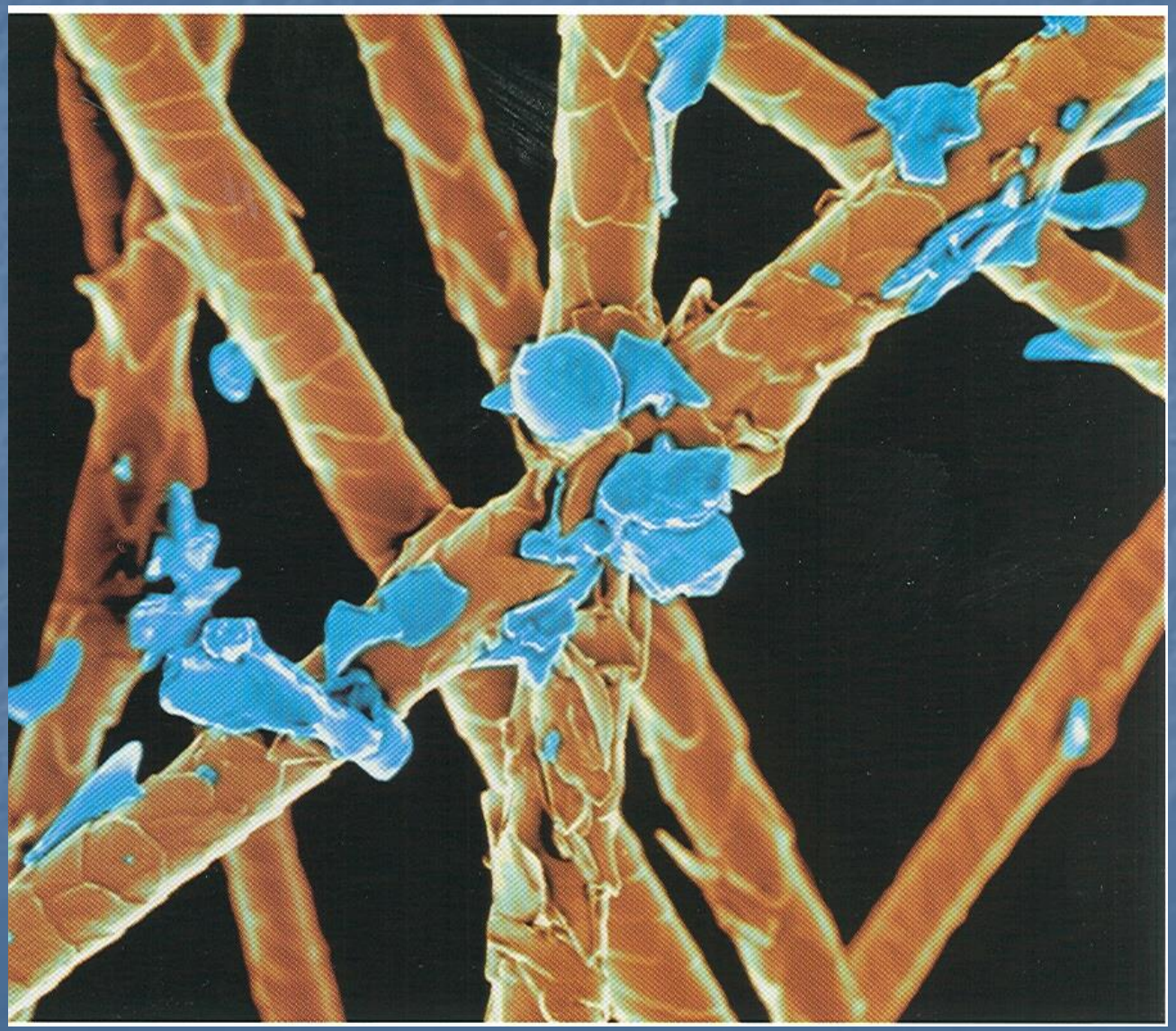
Food allergy

- True IgE mediated allergy eg fish, peanut
- Intolerance eg lactose, caffeine or histamine in foods
- Food aversion
- Much non-scientific and popular belief with no basis eg Multiple chemical sensitivity

- Children
  - Hen egg white
  - Cows milk protein
  - Wheat
  - Peanuts
  - Bony Fish
  - Citrus
  - Soya protein
- Adults
  - Bony Fish
  - Shellfish
  - Peanuts
  - Tree-nuts
  - Tomatoes
  - Chocolate
  - Red wine

Cat hair and skin cells

It is not the actual animal fur or feathers that trigger the immune respons
but the animal dander (dead skin cells) and saliva. A particular protein foun
in cat saliva causes an allergic reaction in many sufferers of airborne allerg



Bee and wasp allergy

- Mild to life threatening
- Approx 4 anaphylaxis deaths per yr in UK
- Sensitisation to insect venom can occur after a single sting

- Most stings from wasps
- Bees in high risk groups
- Identify as bee sting left in skin

- Bee: enzyme phospholipase (Api m II)
- Wasp: enzyme antigen 5 (or Ves g V)
- Only occasional cross reactivity to insect venom enzyme hyaluronidases

Venom Desensitisation Immunotherapy

- Highly successful for severe generalized venom allergic reactions
- Useful for Beekeepers, Horticulturists, Gardeners and Farmers who find it difficult to avoid stinging insects
- Injections are carried out at weekly intervals during the initial treatment phase and then monthly for a further 3 years during the maintenance phase

- By the end of the treatment, the patient is able to tolerate 100ug of venom, the equivalent of two bee or wasp stings, with no adverse reaction

- Injection Immunotherapy should only be performed in specialist hospital-based clinics with readily available resuscitation equipment and the patient should be observed for one hour after each injection

Table 2. Risk of Anaphylactic Reactions to Hymenoptera Stings after an Initial Event.

Patient History*	Approximate Risk of Anaphylaxis (%)†	Immunotherapy If Skin Test or in Vitro Test Is Positive for Antibodies
Unknown history	3	No
Large local reactions	10	No
Cutaneous anaphylaxis in child	10	No
Systemic anaphylaxis in child	50–60	Yes
Anaphylaxis in adult	50–60	Yes
Receiving immunotherapy	2	Not applicable

* The risk in the general population refers to the risk in adults; the risk may be lower in children. Large local reactions are defined as persistent swelling of up to a week's duration; cutaneous anaphylaxis in a child is characterized by pruritus, urticaria, or angioedema. The risk of anaphylaxis for adults with cutaneous reactions only may be as low as it is for children, but this is yet to be determined.

† The data in this table are from Golden,[7] Settipane and Boyd,[8] Chaffee,[9] Golden et al.,[10] Graft et al.,[11] Schuberth et al.,[12] Hunt et al.,[13] and Golden et al.[14]

Immunotherapy

- Subcutaneous and oral
- 1911 hayfever treated by injecting pollen extracts
- Used more in US and Europe in allergic rhinitis
- Option in grass pollen allergic rhinitis and for bee/wasp sting anaphylaxis in UK

- 1986: immunotherapy practically halted in UK with a damning *CSM* report
- This report cautioned against the use of immunotherapy in general practice and cited 26 anaphylactic deaths over 30 years
- Mainly inappropriate use and poor practice in uncontrolled asthmatics

Mechanism of action

- Unknown
- Hypothesised that specific "IgE blocking" antibodies were produced
  - as during successful immunotherapy an initial increase in specific IgE was followed by an IgE fall and compensatory rise in IgG (a blocking antibody)
- Then postulated that specific IgG_4 antibodies where induced towards the offending allergen
- Also see an associated ↓ in mucosal mast cell numbers and ↓ in antigen-induced eosinophil migration to the site of inflammation
- Immunotherapy modulates the T-helper cells
  - causing switching from predominantly TH2 (IgE inducing) to predominantly TH1 (IgG inducing) subsets and as a result of this, allergen-specific IgE falls with successful immunotherapy

Effects of hyposensitization therapy

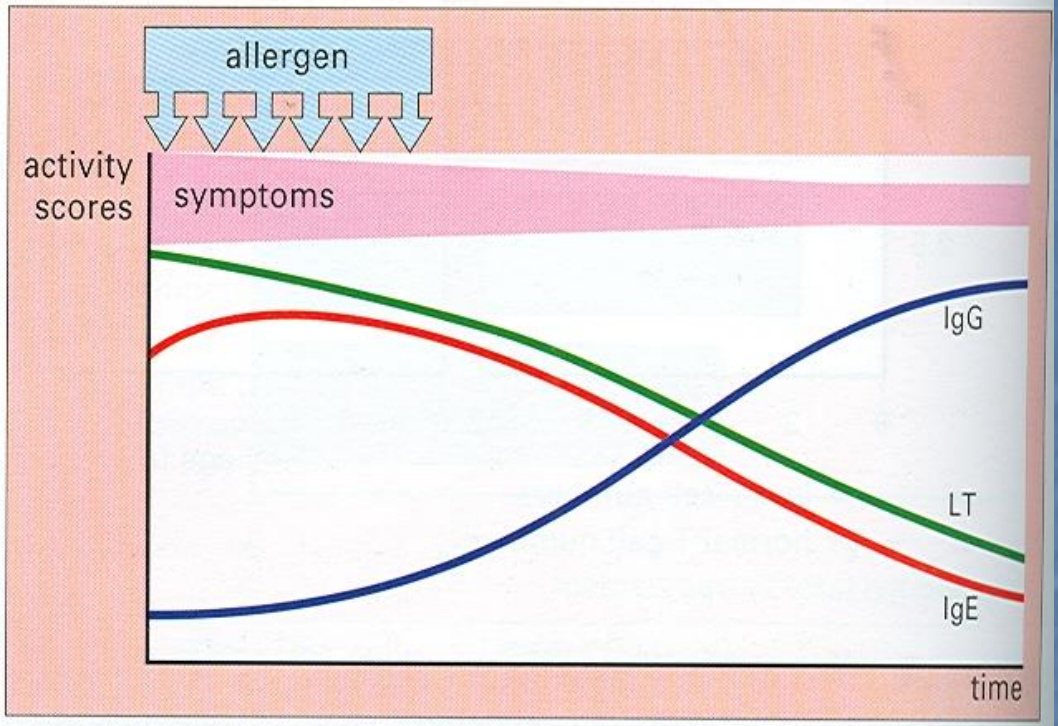


Fig. 23.28 Classical hyposensitization therapy involves repeated injection of increasing doses of allergen. There is an increase in antigen-specific IgG accompanied by a fall in antigen-specific IgE. This fall was thought to be due to an increase in activity of suppressor T cells, which is reflected in reduced antigen-induced lymphocyte transformation (LT) *in vitro*. It may also be due to a shift in the T_H1/T_H2 balance of the immune response to allergen.

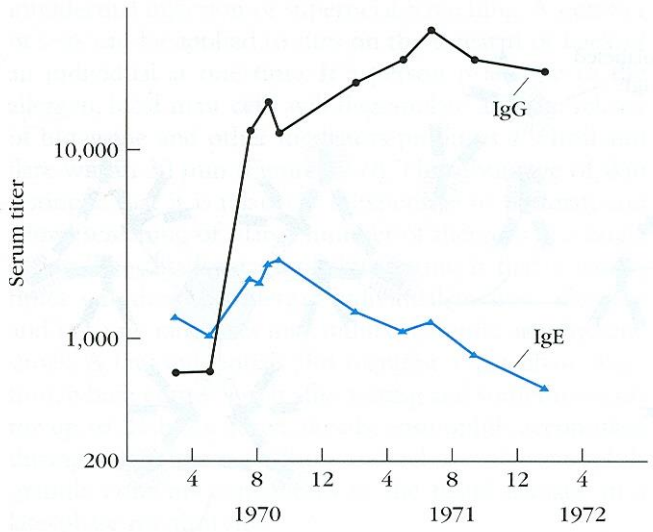
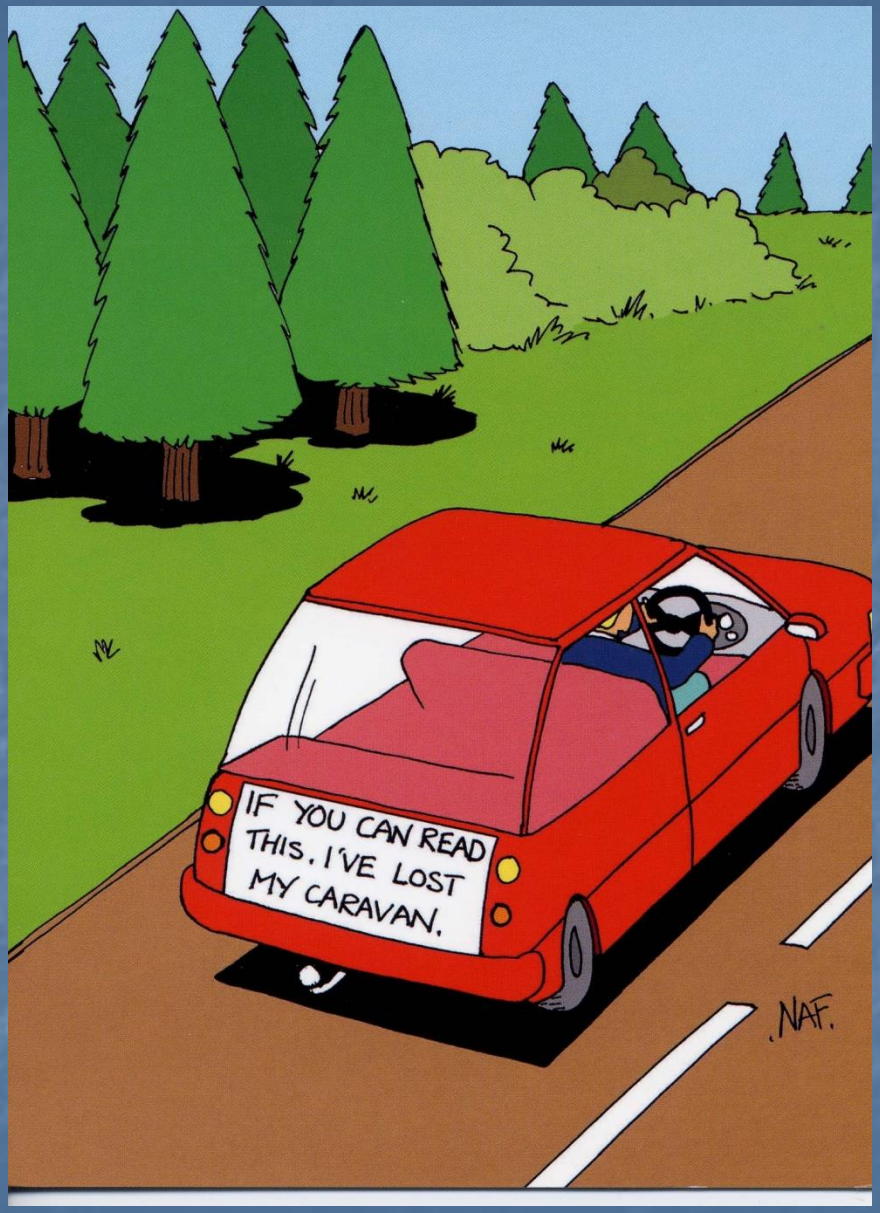


FIGURE 17-11

Hyposensitization treatment of type I allergy. Injection of ragweed antigen periodically for 2 years into a ragweed-sensitive individual induced a gradual decrease in IgE levels and a dramatic increase in IgG. Both antibodies were measured by a radioimmunoassay. [Adapted from K. Ishizaka and T. Ishisaka, 1973, in *Asthma Physiology, Immunopharmacology and Treatment*, K. F. Austen and L. M. Lichtenstein (eds.), Academic Press.]


IF YOU CAN READ THIS, I'VE LOST MY CARAVAN.
NAF.


I THINK I'M ALLERGIC TO CHILDREN!

Use

- Confirm IgE mediated allergy by skin prick tests or Sp IgE levels
- S/c Immunotherapy has been mostly used in the UK to treat grass pollen, seasonal allergic rhino-conjunctivitis and Wasp/Bee sting anaphylaxis
- Housedust mite, Cat and Birch Pollen allergic rhinitis can only be treated with immunotherapy on a strictly "named-patient basis" (directive from the Medicines Control Council of the UK)
- "Grazax" an oral tablet form of grass pollen desensitisation immunotherapy is now available the UK

- The fewer allergens used in immunotherapy, the better the result
- Vaccine mixtures tend to be unstable and should not contain mixtures of unrelated allergens
- People with a single specific inhalant allergy derive most benefit from immunotherapy
- But 2 inhalant allergens can be administered at the same time, at different injection sites

Contraindications

- > 50ys and < 5yrs
- IHD
- Hyperthyroidism
- Auto-immune disease
- Malignancy
- Off β blockers (lessen adrenaline effects)
- Not if have wheeze
- Relative contraindications
  - Pregnancy
  - Eczema
  - chronic uncontrolled asthma
  - food allergy
  - mould allergy

S/c immunotherapy

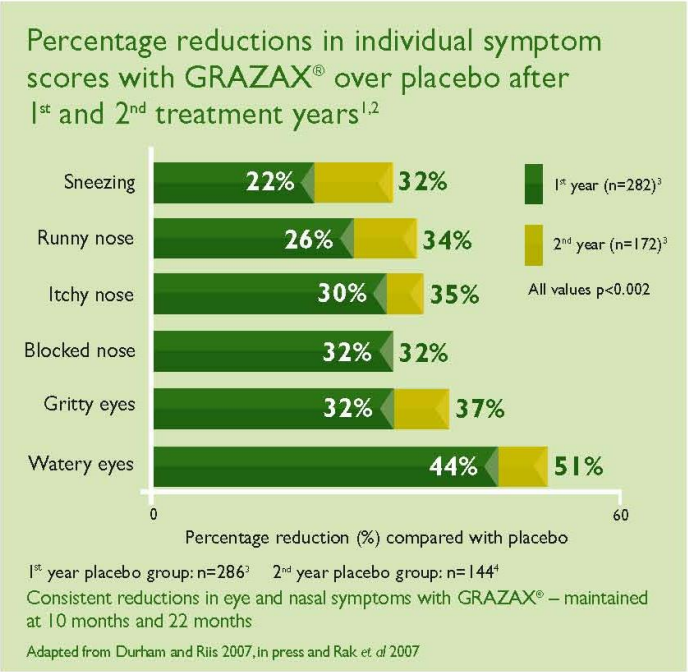
- In hospital with resus kit present
- S/c to upper arm once a week
- dose is doubled weekly until a state of tolerance to the allergen is achieved, usually at 15/52
- Grass pollen immunotherapy should be commenced pre-seasonally to reach maintenance before the season
- Maintenance injections 4 to 6-weekly for period of 3 years to complete the immune modulating process
- Observe for 1 hour
- Avoid sport, exercise, alcohol and hot baths for 8 hours
- Up to 50% ↓ in symptom scores and 80% ↓ in Rx requirements

Oral immunotherapy

- Grazax available for adults in the UK for grass pollen induced hayfever and allergic rhino-conjunctivitis
- Contains an extract of Timothy Grass (Phleum Pratense) 75000SQ-T
- Safe and less likely than S/C to cause any adverse reaction
- 1st dose must be administered under the supervision with 20-30 minutes observation
- subsequent doses at home
- one tablet daily should commence at least 2 months before the grass pollen season and continued throughout the grass pollen season for maximal benefit
- The treatment is stopped in the autumn/winter and then recommence at least 2 months prior to each subsequent grass pollen season
- Main drawback is cost - each tablets cost £2 or £67 per month for 4-5 months

GRAZAX® IMPROVES BOTH EYE AND NASAL SYMPTOMS

SYMPTOM SCORES WERE BASED ON CHANGES IN SIX SYMPTOM DOMAINS



- GRAZAX® reduced mean rhinoconjunctivitis symptom scores by 36% (median reduction 44%) in the 2nd treatment year compared with placebo[3]
- GRAZAX® significantly improved both eye and nasal symptoms compared with placebo[2]
- Symptom score reductions were accompanied by lower usage of symptomatic medication compared with placebo[2]
- Patients taking GRAZAX® showed improvement in hay fever symptoms compared with patients taking placebo and standard medications alone[2,3]

Both groups had open access to standard medications (antihistamines and nasal steroids)

Placebo group = placebo GRAZAX® + standard medications; GRAZAX® group = GRAZAX® + standard medications. Design: Double-blind, placebo-controlled, parallel-group, multicentre trial. Number of patients: 634, aged 18–64 years. 546 subjects completed the 1st treatment year. Treatment: GRAZAX® or placebo, once-daily, administered at least 16 weeks prior to and throughout the grass pollen season of 2005. Rescue medication was scored daily: desloratidine 5mg once-daily = 6, budesonide nasal spray (up to 32µg per day) = 1 per spray, prednisone (up to 50mg once-daily) = 1.6 per 5mg.

In the 2-year follow-up, 351 adult participants were continued into the 2nd treatment year. 189 subjects were treated with GRAZAX®, 162 received placebo once-daily for an average of 22 months.

CUTS THE SYMPTOMS, TREATS THE CAUSE

GRAZAX®
Phleum pratense

References: 1. Rak S *et al.* Poster 656 presented at: XXVI Congress of the European Academy of Allergology and Clinical Immunology. June 9–13, 2007. Göteborg, Sweden. 2. Durham and Riis. *Allergy* 2007; In Press. 3. Emminger W *et al.* Poster 663 presented at: XXVI Congress of the European Academy of Allergology and Clinical Immunology. June 9–13, 2007. Göteborg, Sweden. 4. Data on file. ALK-Abelló, 2007.

Prescribing Information can be found on the back page.

Outcome & benefits of successful immunotherapy

- S/C regular injections for at least 3 years
- Limited knowledge exists about the optimal duration
- Grass and Birch Pollen benefit for at least 6 years
- Housedust mite allergy the duration of clinical response may be shorter
- Between 7 - 17% of bee-venom allergic people will relapse 1-2 years after completion of successful injection immunotherapy
- Because of this small risk of relapse, advisable for patients to carry emergency antihistamines or adrenaline after completing their immunotherapy

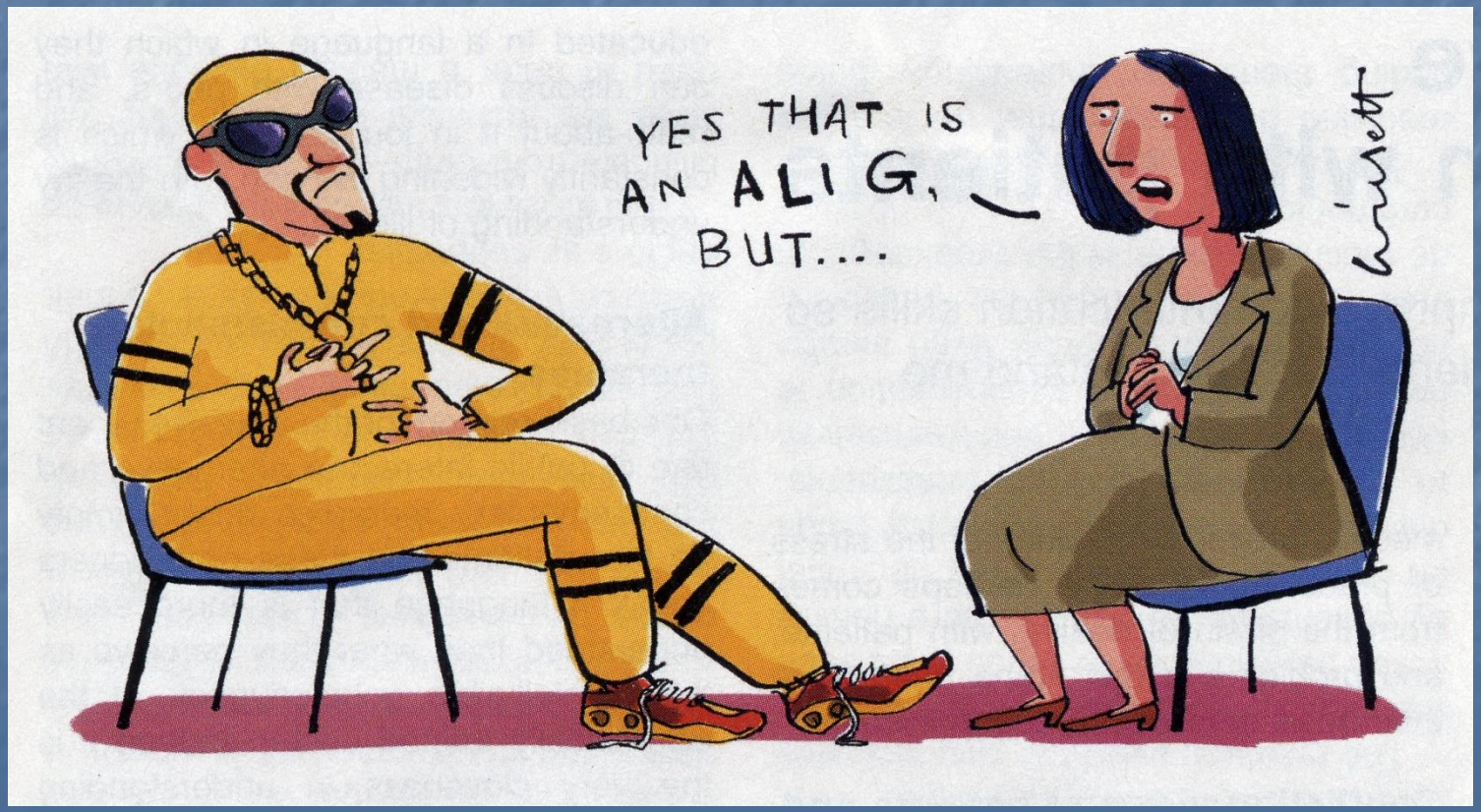
Enzyme Potentiated Desensitisation

- Different procedure which employs an enzyme (B-glucuronidase) mixed with numerous allergens and then injected into the skin

- No benefit in double blind RCT

(Radcliffe M.J. et al, BMJ; 2003: 327: 251)

Could you use an Epipen® if you had to?



Epipen®

Step 1

Remove pen from holder

Step 2

Hold pen firmly in hand

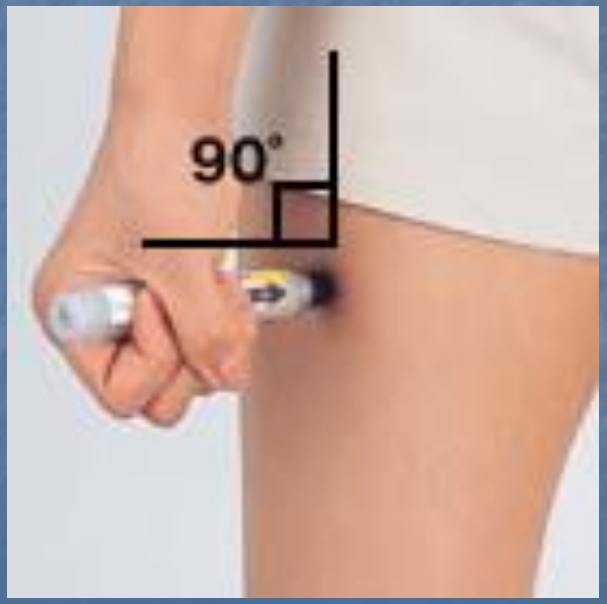
Epipen®

Step 3

Remove the grey cap from the top of syringe

Step 4

Swing and push the syringe into outer thigh



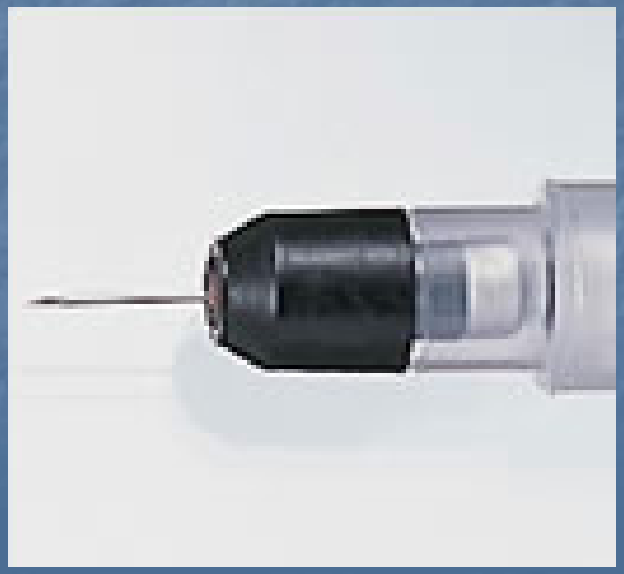
Epipen®

Step 5

Hold against leg for 10 seconds, then rub the area of injection

Step 6

Check that the needle is now showing



Epipen®

Step 7

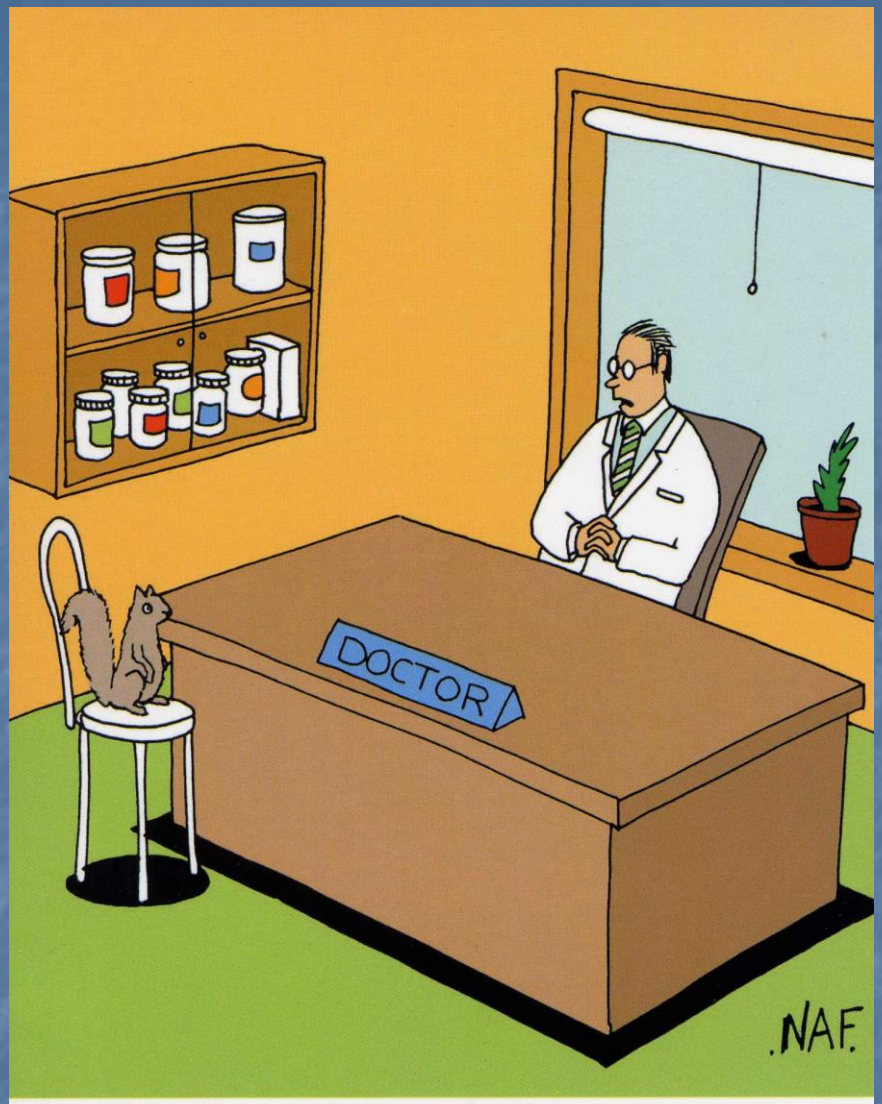
Push needle against hard surface to bend it back on itself

Step 8

Put syringe back in container and take it with you when you seek medical advice

Honey

- Anecdote
- 2002 Connecticut N=36
  - Local raw honey vs national brand vs corn syrup
- Allergy diary no differences seen
- Cases of anaphylaxis rare but have occurred
  - 1 reported death in France



"Bit of a bummer really,
you've got a nut allergy."