IMPERIAL

Anaphylaxis

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Thomas Curtis

A 27 year old in good health.

Toothache → emergency dental appointment – abscess!

A temporary filling was provided, prescribed penicillin to treat the abscess.

Within 1 hour of taking the first tablet, Thomas began to feel unwell.

- Nausea, dizziness.
- Hot itchy skin.
- Puffy skin around the eyes with obvious rash.

Thomas is taken to his nearest emergency department.

Abscess around apex of root.

Hospital - 1

- By the time they arrived at the hospital, Thomas was quite breathless and faint, and was brought into the emergency department on a wheelchair.
- He was dealt with as a priority.
- He was lain down on a couch with legs raised, and given an intramuscular injection of adrenaline.
- A blood pressure monitor was attached to his arm, a drip was set up, and further injections were given.
- He was kept in hospital under close observation overnight, by which stage he was feeling considerably better.

Chelsea & Westminster

Hospital - 2

- The duty officer suspected a penicillin allergy.
- Thomas had penicillin on a number of occasions previously without obvious ill effects. Last time was two years ago when he had been involved in a bicycle accident.
- Penicillin administered as a precaution against wound infection, and because he was concussed the casualty officer had given the antibiotic intravenously.
- Thomas was advised that he had acquired an allergy to penicillin, that had resulted in a severe anaphylactic reaction.
- Repeat exposures likely to be problematic - he should avoid taking the drug in the future.
- He was given advice on the names of other antibiotics that contained penicillin or penicillin-like drugs, and was recommended to wear a bracelet advising of this allergy in case of future accidents.

Questions to be addressed (in groups)

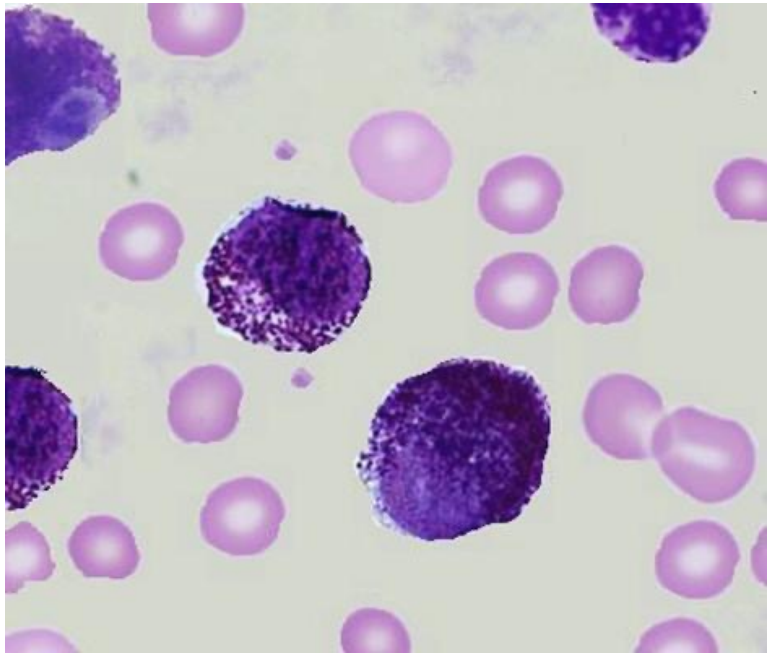
Work out the possible cell and molecular scenario by which the patient became allergic, and responded to penicillin with the symptoms of anaphylaxis.

- What type of cell causes these symptoms?
- What is the signalling molecule involved?
- What immunoglobulin class is likely to be involved?
- What causes the rashes and puffy skin?
- Why should adrenaline have been given?
- What sorts of drugs might have been in the subsequent injections?
- Why did the patient feel faint?
- Why was blood pressure monitored in hospital?

Take home messages - 1

What type of cell causes these symptoms?

- The mast cell.
- Released as a progenitor from bone marrow.
- Homes to connective and mucosal tissues where it matures.
- Noted for its many granules.

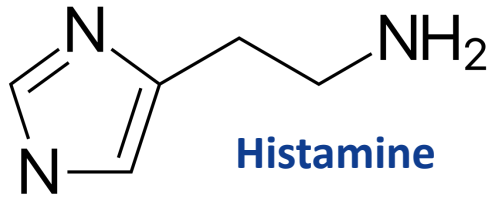


By Ayman Qasrawi
https://commons.wikimedia.org/w/index.php?curid=35421736

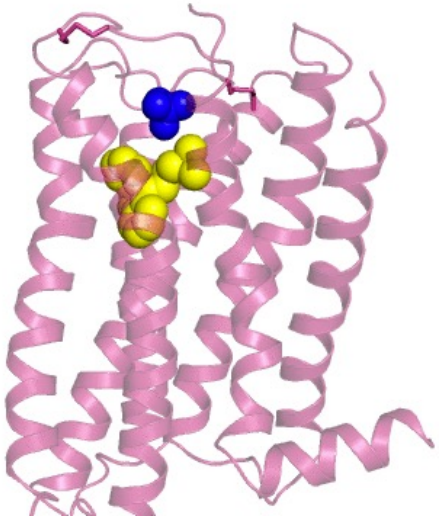
Take home messages - 2

What is the signalling molecule involved?

- Mast cells are widely distributed throughout the body both in **connective tissue** (e.g. under the skin) and in association with **epithelial mucosae** (e.g. the respiratory and intestinal epithelia).
- Mast cell granules contain several inflammatory mediators, notably **histamine** and **leukotrienes**.
- Inflammatory mediators act principally on **blood vessels** and **smooth muscle** which express specific histamine receptors (GPCRs).



Histamine



Histamine receptor

Take home messages - 3

What immunoglobulin class is likely to be involved? PoM Primer - Antibodies

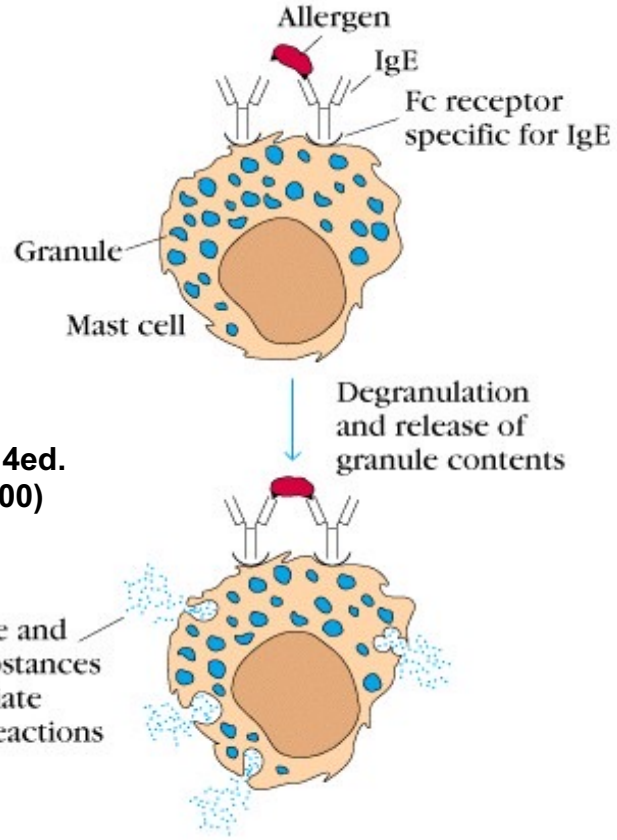
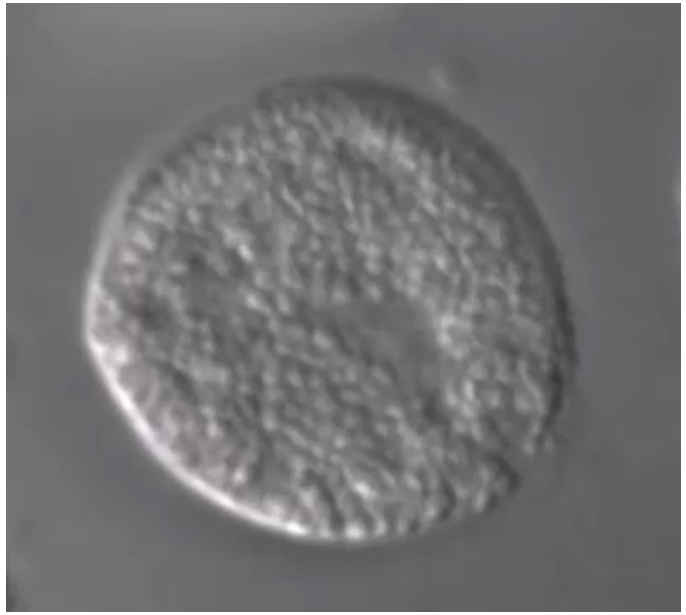


Figure 4-16
Kuby Immunology, 4ed.
(©W.H. Freeman 2000)

- IgE binds with high affinity to Fc receptors of mast cells.
- Present at extremely low levels in blood.
- Produced in response to parasitic infections and in allergic diseases.
- Cross-linking by antigen triggers mast cell activation and histamine release.



Movie kindly provided by Shiro Kanesagawa, ECI, Japan.

Take home messages - 4

What causes the rashes and puffy skin?

- In connective tissue, histamine causes **dilatation** of vessels with increased blood flow to the surface and increased movement of fluid out of the blood stream (**oedema**).
- Rash (urticaria) is a acute response to allergen raised lump or wheal.
- Caused by animal hair, proteins in natural latex, certain chemicals, substances in insect and plant stings.

Urticaria - James Heilman, MD CC-BY-SA 3.0

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Take home messages - 5

Why should adrenaline have been given?

- Anaphylaxis results from a **systemic** response to the allergen.
- Dilatation of peripheral blood vessels results in a dramatic drop in blood pressure (**hypotension**) which can affect organ function: this is known as **shock**.
- An injection of **adrenaline** will act to constrict peripheral blood vessels and redirect blood to the organs.

Take home messages - 6

What sorts of drugs might have been in the subsequent injections?

In the mucosal tissues of the lung, histamine release causes constriction of the bronchi resulting in breathing difficulties. The patient will respond with an increase in both respiratory and heart rates.

There may also be symptoms of nausea, abdominal cramps or diarrhoea from the effects on the intestines.

Medications that may be used:

- Anti-histamines e.g. diphenhydramine.
- Corticosteroids e.g. hydrocortisone.

If breathing problems persist, oxygen may be necessary and bronchodilators may be given via an inhaler e.g. salbutamol.

Take home messages - 7

Why did the patient feel faint?

- Due to the dramatic drop in blood pressure (hypotension).
- **Syncope** (fainting) is a temporary loss of consciousness usually related to insufficient blood flow to the brain.
- Note that on arrival at A&E, Thomas was initially laid down on a couch with his legs raised to counteract this.

Take home messages - 8

Why was blood pressure monitored in hospital?

- Monitoring of blood pressure provides a reliable indication of recovery.
- Occasionally the symptoms return (usually within hours of the initial reaction).
- This is known as **biphasic anaphylaxis**.
- Patients with moderate respiratory or cardiovascular compromise should be observed for to up to 8-10 hours before discharge.

Long term management of anaphylaxis

- Long term treatment is largely by avoiding known allergens.
- For those difficult to avoid completely (such as wasp stings, or nuts where small traces may contaminate apparently innocent foods) the patient may be given adrenaline in a self-injection “pen” e.g. EpiPen®, Emerade®.

Simons et al, *World Allergy Organ J* 2011;**4**:13–37

1-POM-3-9: Hypersensitivity: Outline the mechanisms by which antibodies, immune complexes and T-lymphocytes can cause tissue damage and inflammation in hypersensitivity reactions