

IMMUNOLOGICAL DISEASES

AN INTRODUCTION TO HYPERSENSITIVITY

Allergy & hypersensitivity

HYPERSENSITIVITY

= harmful immune responses



autoimmunity
(*self* antigen)



allergy
(*foreign* antigen)

Classification of Hypersensitivity

	Type	Mechanism	Example
Anaphylactic hypersensitivity	I	IgE mediated	Systemic anaphylaxis eg peanut allergy Asthma
Cytotoxic hypersensitivity	II	Antibody mediated	Haemolytic disease of the newborn
Immune complex hypersensitivity	III	Immune complex mediated	Arthus reaction Glomerular nephritis
Cell-mediated hypersensitivity	IV	Cell mediated (delayed)	Contact dermatitis

Type I hypersensitivity (Immediate reaction)

- Dependant on IgE and Mast cells.
- Requires prior sensitisation to antigen.

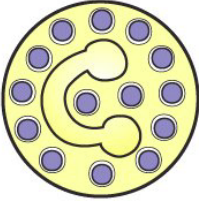
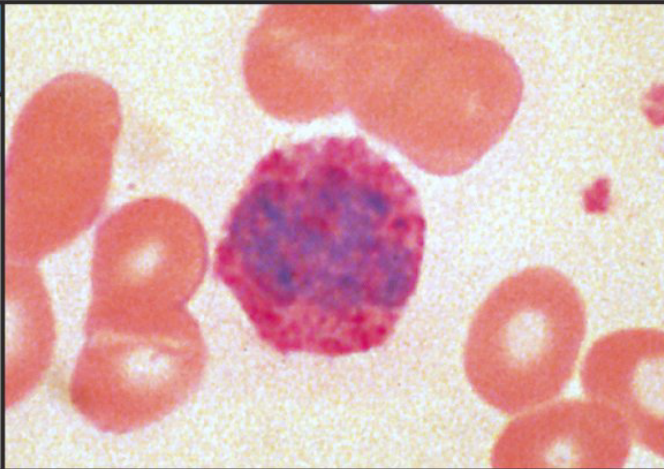
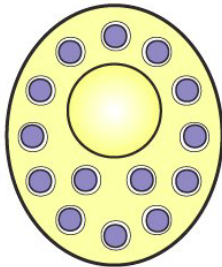
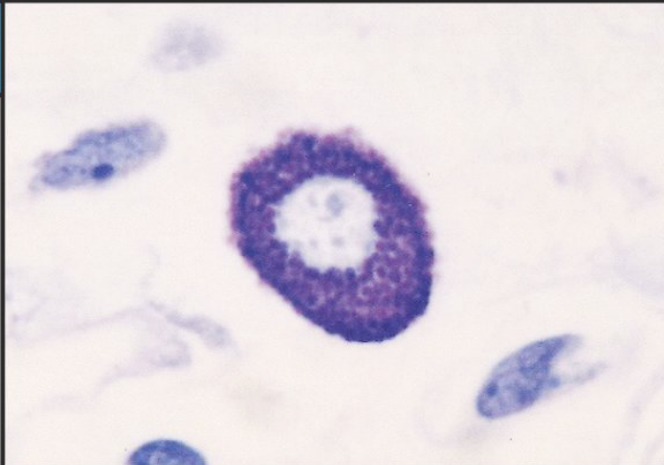
Cell		Activated function
Basophil 		Unknown
Mast cell 		Release of granules containing histamine and other active agents

Figure 1-4 part 3 of 3 Immunobiology, 6/e. (© Garland Science 2005)

Response of type I hypersensitivity

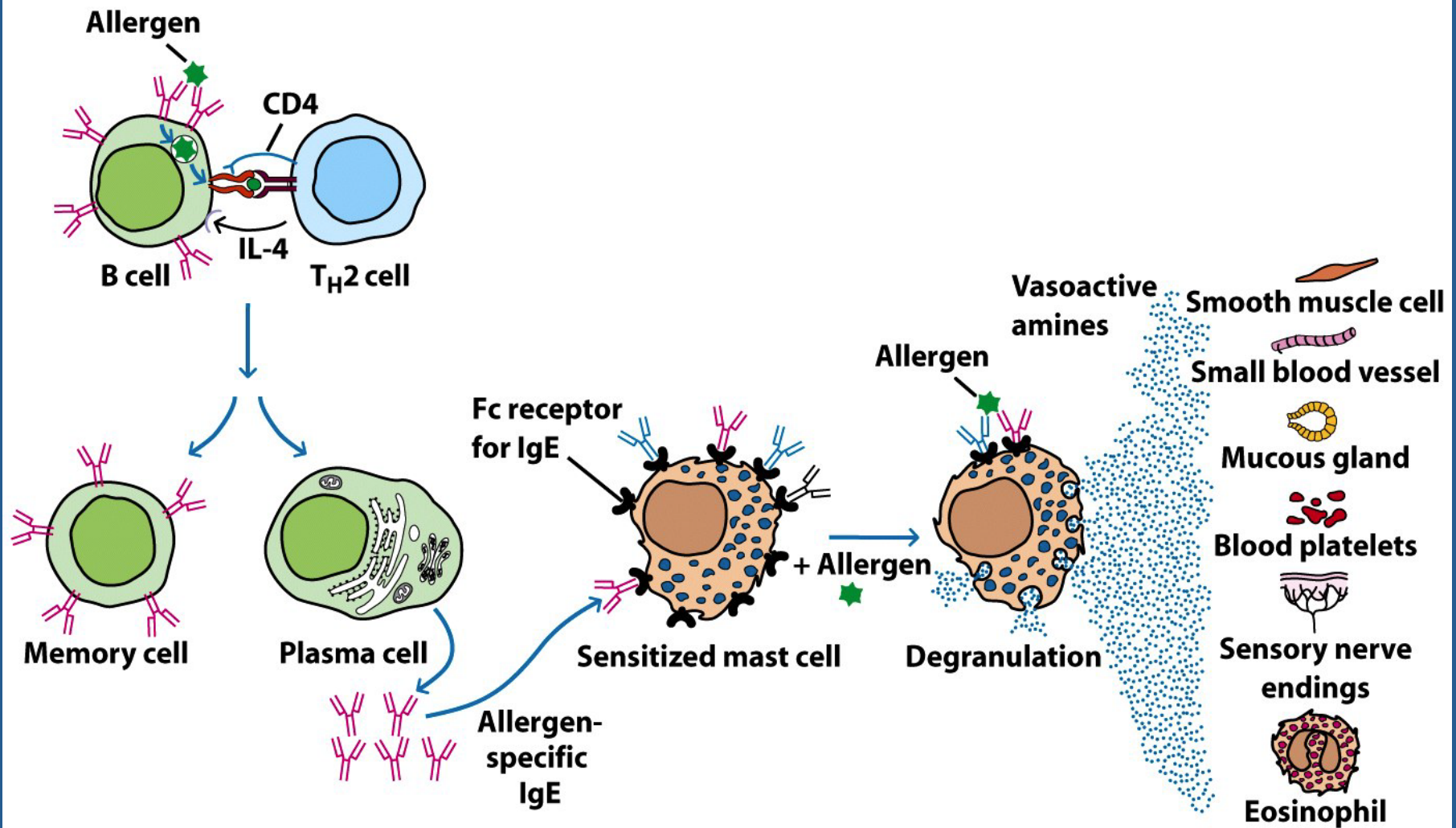
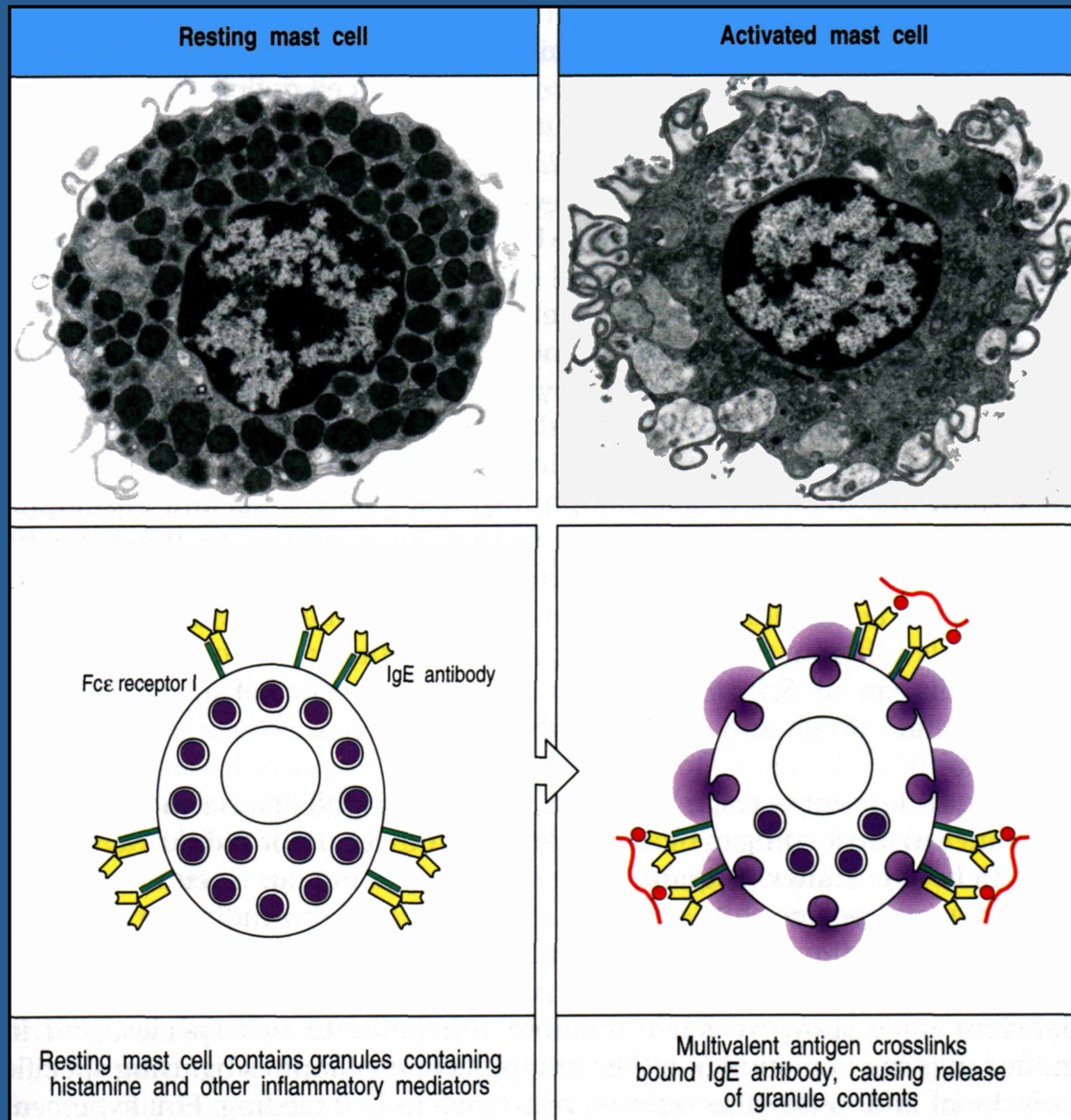
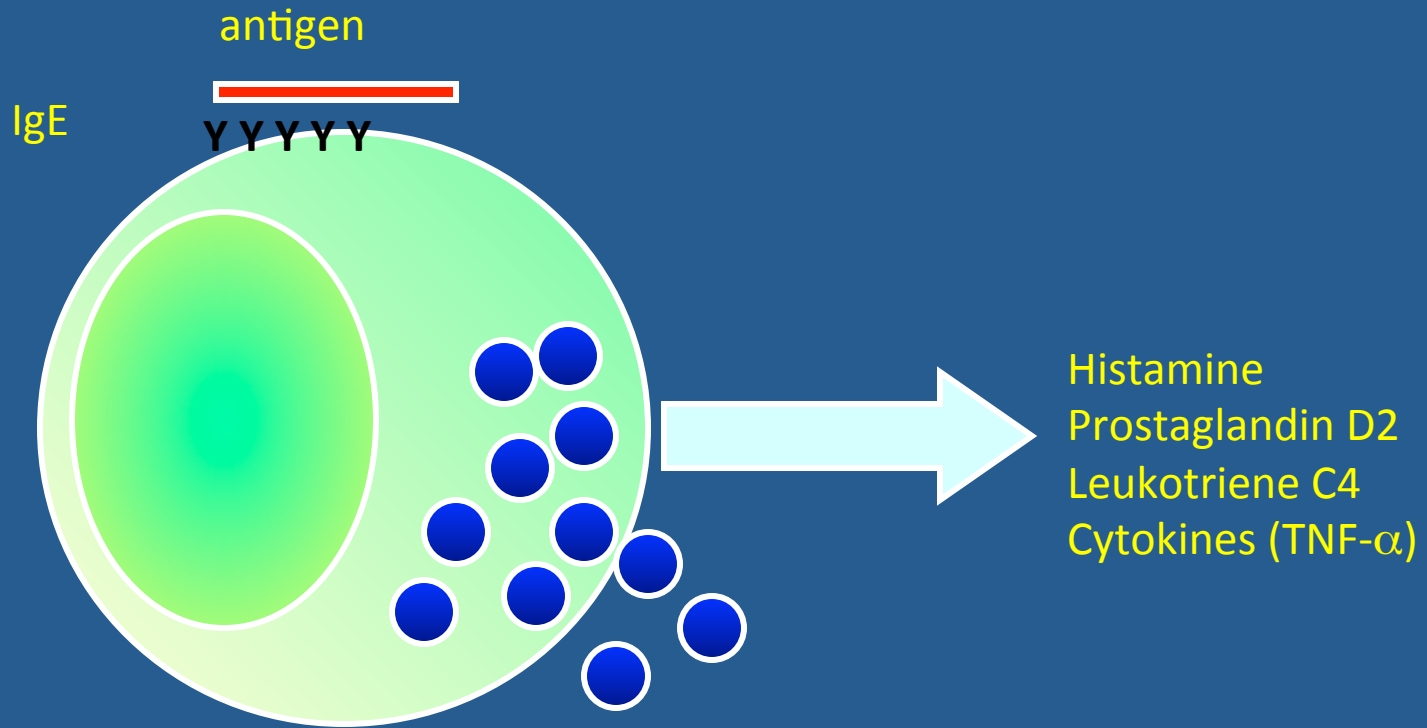


Figure 15-2
Kuby IMMUNOLOGY, Sixth Edition
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Mast cell degranulation



Key Event. Mast cell activation (elicitation phase)



Effector mechanisms

- Mast cell activation:
 - preformed mediators
 - histamine
 - enzymes (*e.g.* tryptase)
 - TNF- α
 - synthesis
 - leukotrienes C4, D4
 - IL-4, IL-5
- Results:
 - vasodilation and increased permeability
 - increased mucus secretion
 - bronchoconstriction
 - Cough
 - chemotaxis of other inflammatory cells

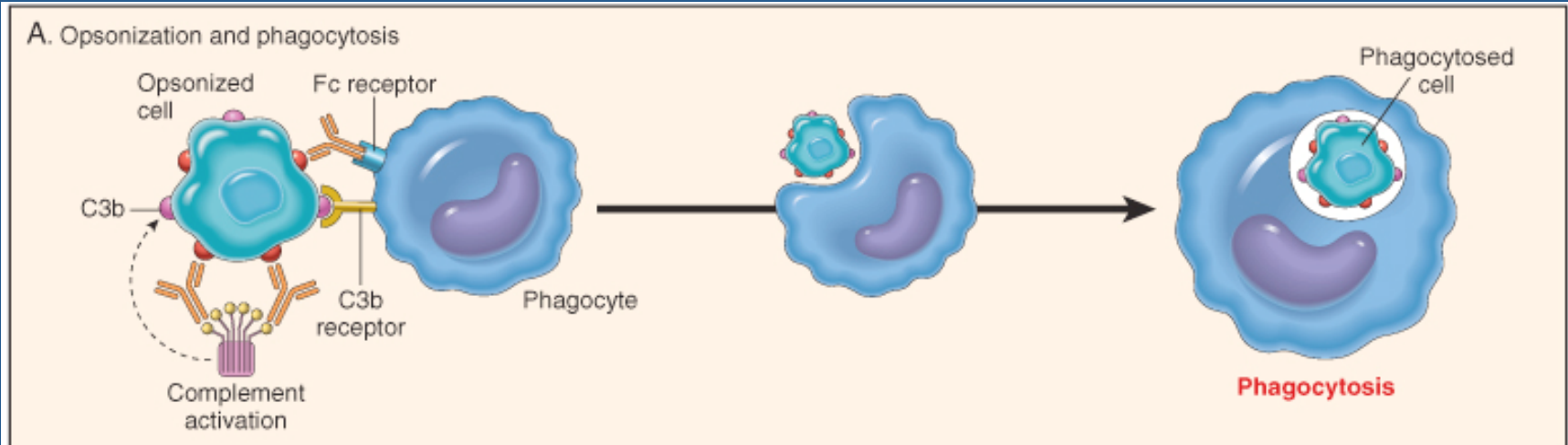
Type II hypersensitivity

- Caused by IgM or IgG antibodies to cell surface and extracellular matrix proteins.
- Abs interact with complement components and effector cells such as macrophages and neutrophils.
- This results in tissue damage via mechanisms normally active against foreign antigens.

EXAMPLES

1. Reactions against incompatible blood transfusions.
2. Autoimmune haemolytic anaemia. Sensitised to patients' own RBCs. Often drug induced.
3. Goodpastures Syndrome. Ab against basement membrane proteins produce nephritis.
4. Myasthenia Gravis. Muscular weakness associated with Abs to acetylcholine receptors.
5. Haemolytic disease of the newborn. Pregnant woman is sensitised to the fetal erythrocytes.

Autoimmune hemolytic anemia



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HAEMOLYTIC DISEASE OF THE NEWBORN (HDNB)

- Occurs when mother has become sensitised to Ag on the infant's erythrocytes. Rhesus D commonly.
- Often Rh –ve mother carrying a second or subsequent rhesus +ve infant.
- Sensitisation of the mother during the birth of the first Rh +ve baby.
- Subsequent children have an increased risk of being affected.

HAEMOLYTIC DISEASE OF THE NEWBORN

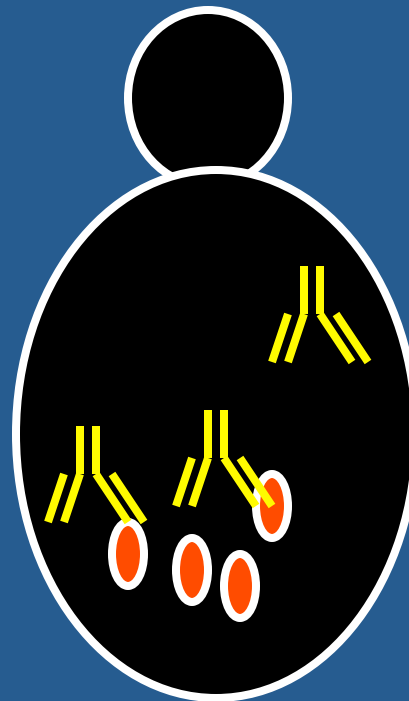
First birth

Postpartum

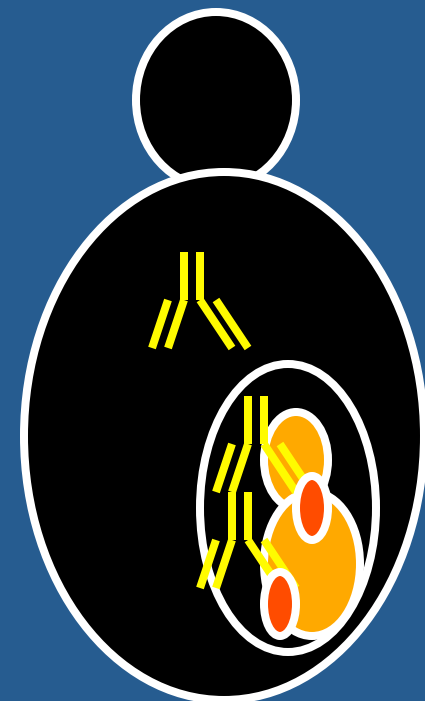
Subsequent pregnancy



Exposure



sensitisation

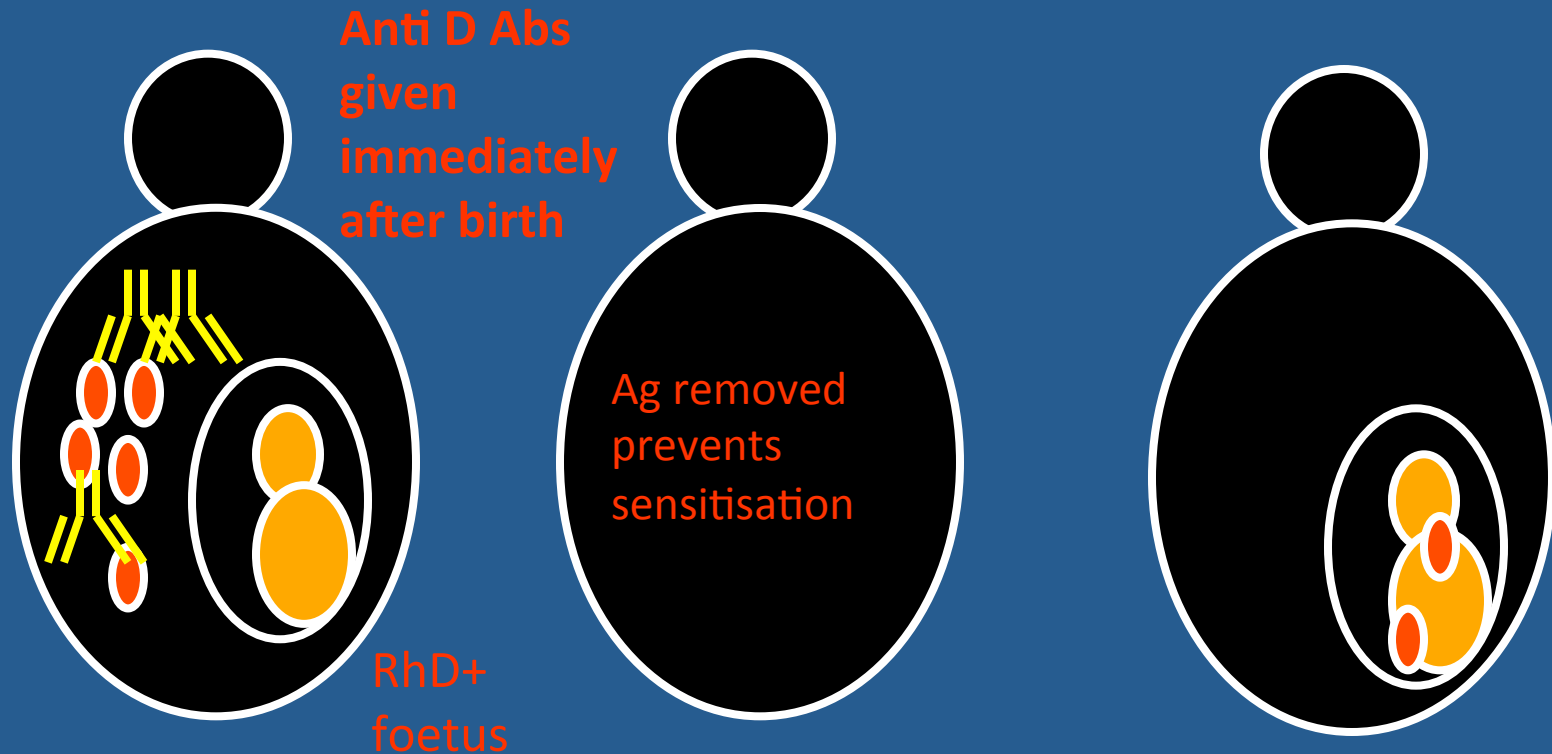


disease

First birth

Postpartum

Subsequent pregnancy

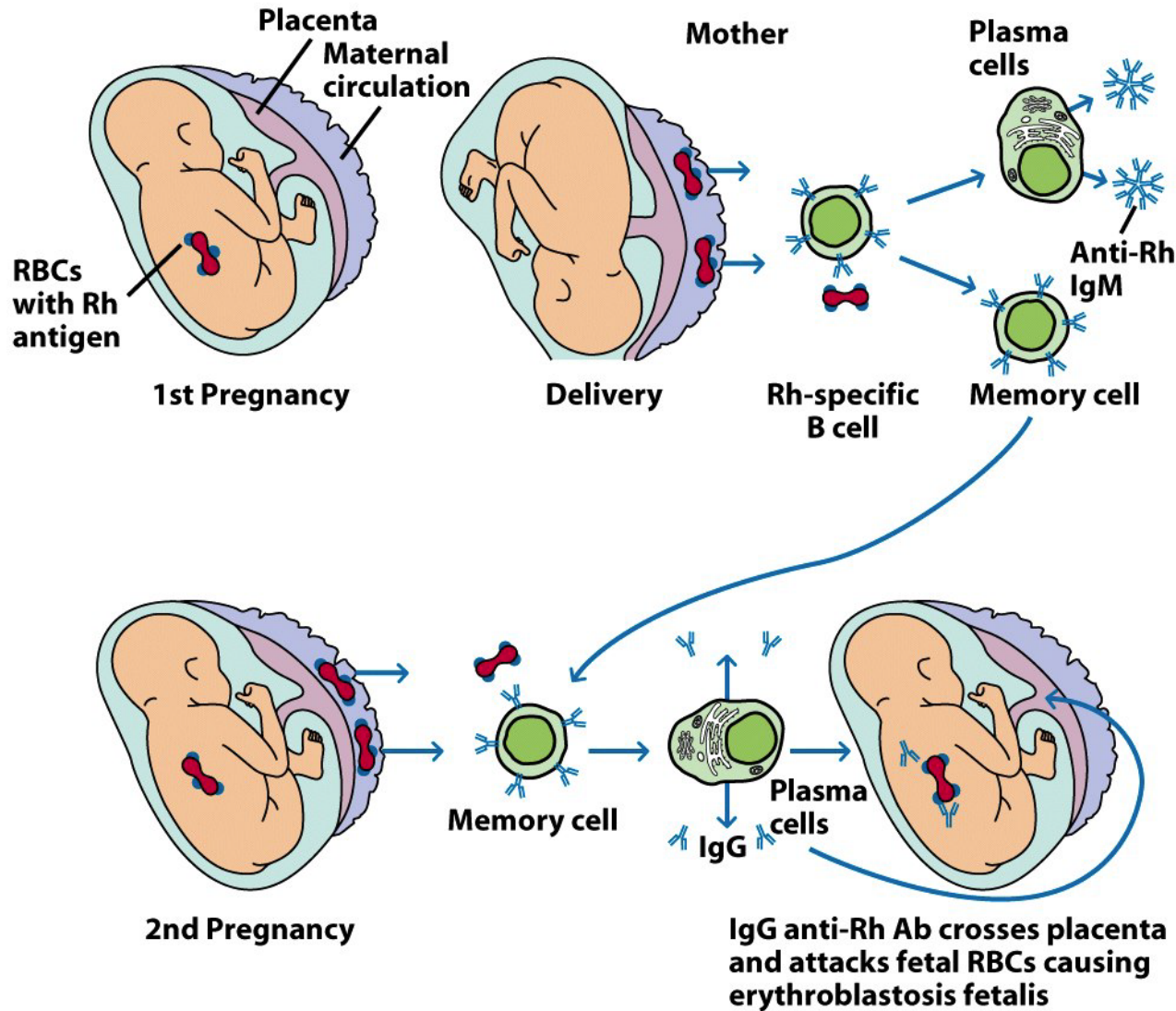


Exposure

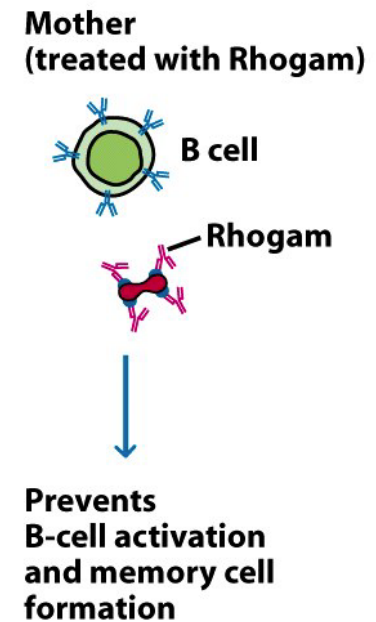
no sensitisation

no disease

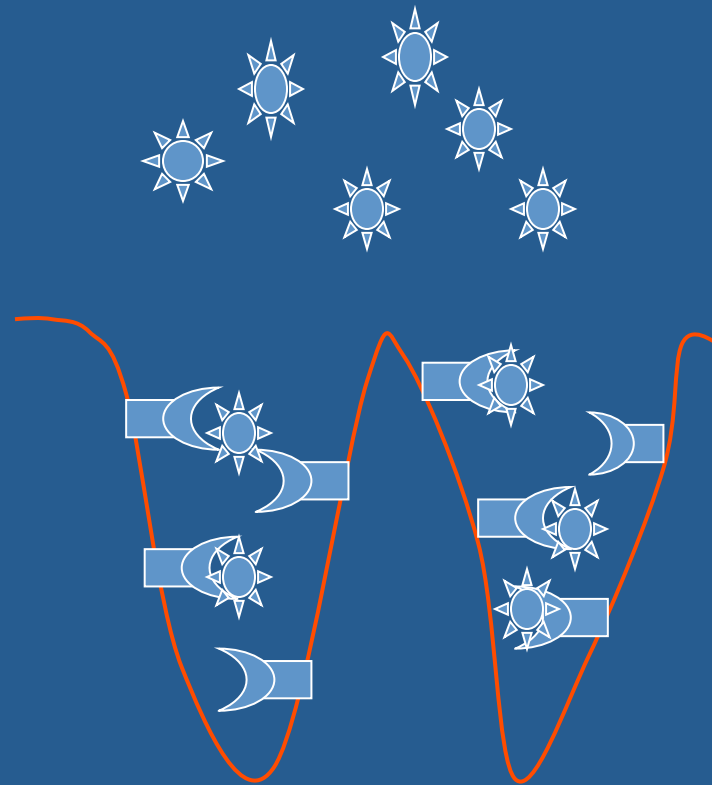
DEVELOPMENT OF ERYTHROBLASTOSIS FETALIS (WITHOUT RHOGAM)



PREVENTION (WITH RHOGAM)



Normal nerve signal

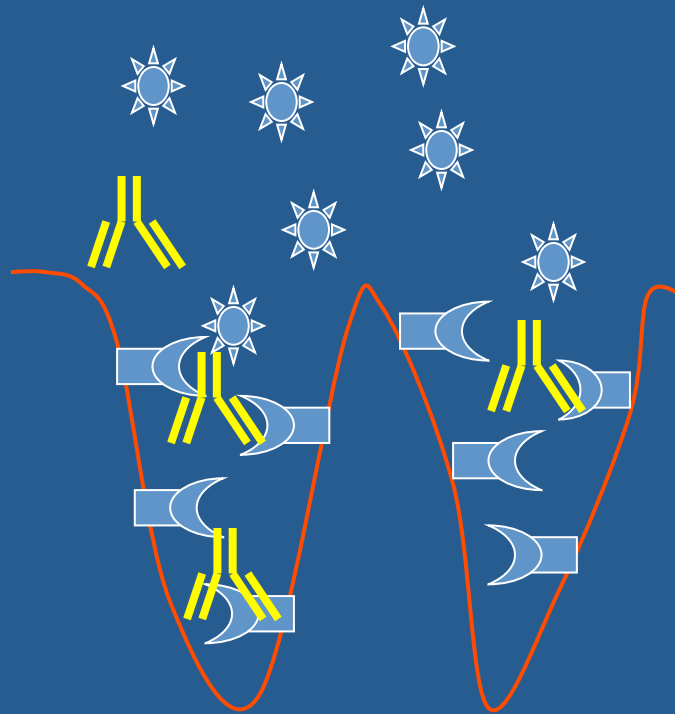


Acetyl choline from
nerve impulse

Acetyl choline
receptors

Muscle fibres

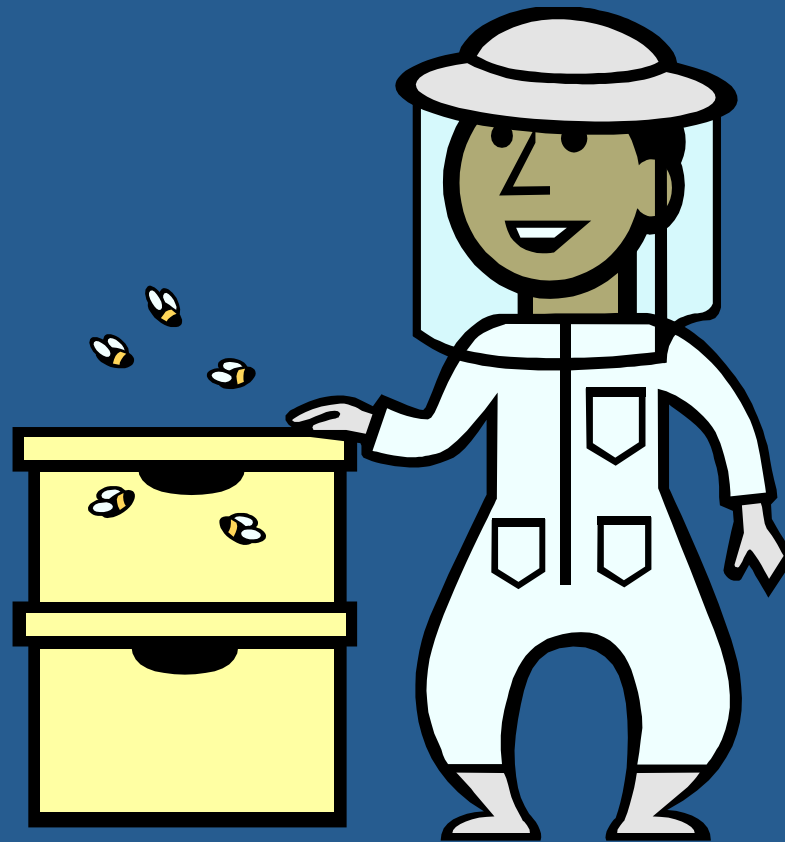
MYASTHENIA GRAVIS

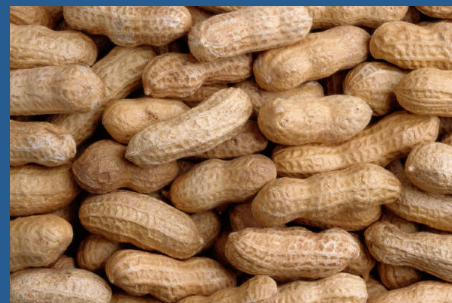


Antibodies to the
receptor block
acetylcholine binding

Muscle weakness from
reduced signal
transmission

Ab against the receptor is only part of the disease process





ANAPHYLAXIS

An immediate, severe, systemic hypersensitivity or allergic reaction, sometimes fatal, usually characterised by at least one or other of the following symptoms, respiratory difficulty, hypotension or circulatory failure. Generalised urticaria and tissue swelling also common.

Mediated by IgE antibodies and Mast cells Immunologically disease.

‘Type One hypersensitivity’

Common causes of anaphylaxis

- Foods
- Serum/vaccines
- Bee and wasp stings
- Drugs
- Latex rubber - gloves

Foods commonly causing anaphylaxis

- Peanuts
- Tree nuts (eg. brazil nut, almond, hazlenut)
- Fish
- Shellfish
- Egg
- Milk
- Sesame

Drugs causing anaphylaxis

- Antibiotics (especially penicillin)
- Intravenous anaesthetic drugs
- Aspirin
- Non-steroidal anti-inflammatory drugs

Urticaria

Raised, erythematous intensely itchy skin eruption caused by IgE-mediated histamine release from mast cells.



Causes: *Drugs*
penicillin
cephalosporins

Food allergens
Environmental allergens
Insect bites
latex

The End