

Immunology and the middle ear

Andrew Riordan



The Immune system is NOT there;

- To baffle medical students
- To keep Immunologists in a job
- To encourage experiments on mice

The Immune system IS there
as a defence against infection.

If some or all of it is not working
there is a high risk of infection.

The immune system

Needs to fight variety of infectious agents (10^{-5} to 10^3 mm). Needs variety of mechanisms:

- Cells and chemicals (Cell-mediated & humoral)
- Specific and non-specific
- Intracellular and extracellular

The immune system

	Humoral	Cell-mediated
Innate/ Non-specific	Complement	Phagocytes
Acquired/ Specific	Antibody	T cells

Non-specific, cellular immunity

Polymorphs

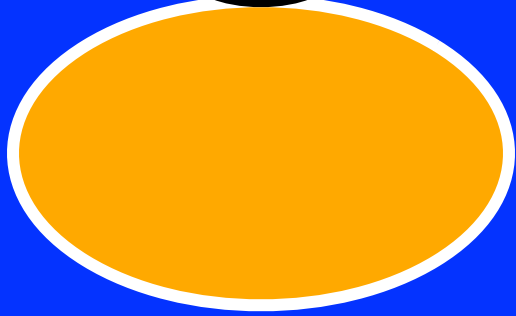
- Main role is phagocytosis
- Adhere to endothelial cells then extravasate

Phagocytes



Phagocytes

← Micro-organism

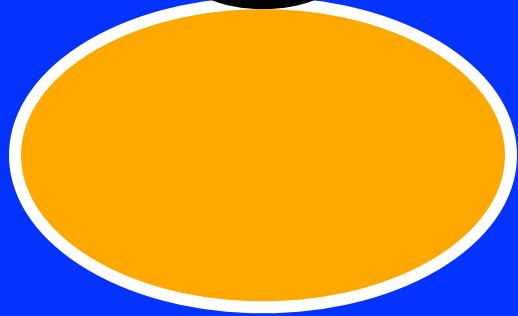


Adherence

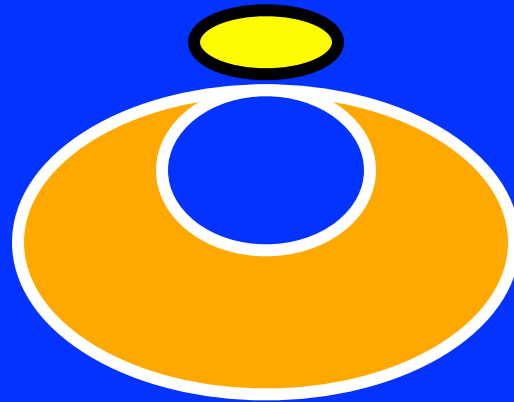
Migration

Phagocytes

← Micro-organism



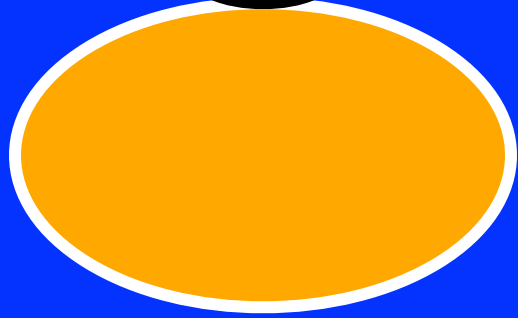
Adherence



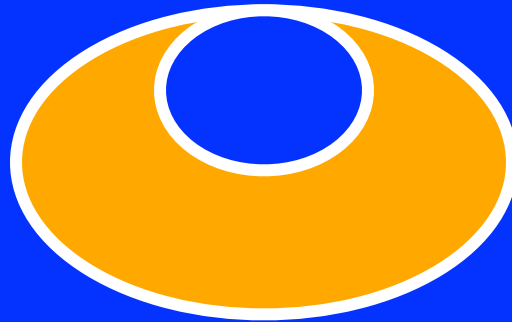
Migration

Phagocytes

← Micro-organism



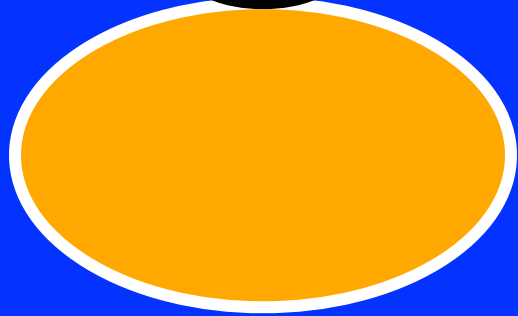
Adherence



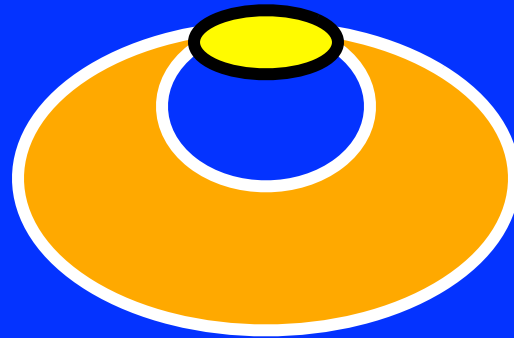
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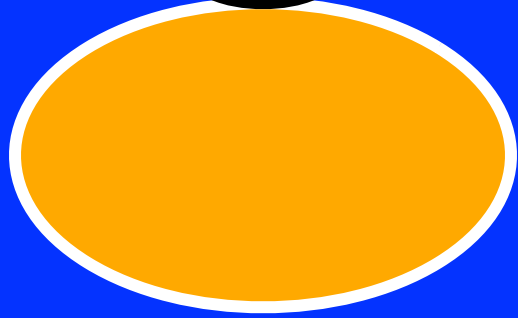
Adherence



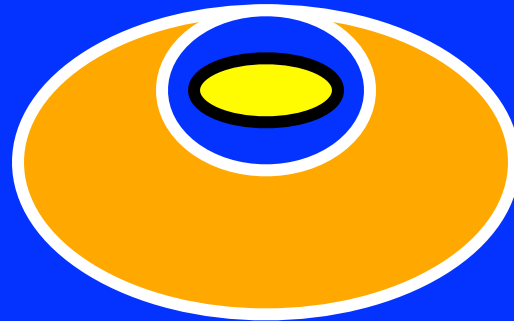
Migration

Phagocytes

← Micro-organism



Adherence

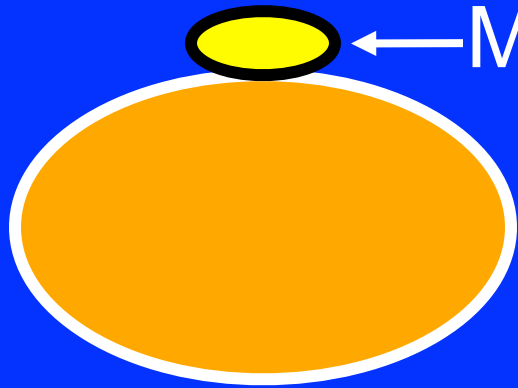


Phagocytosis

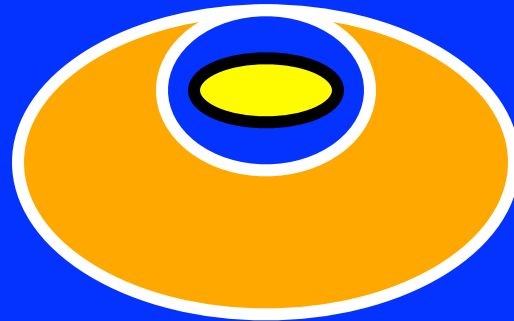
Migration

Phagocytes

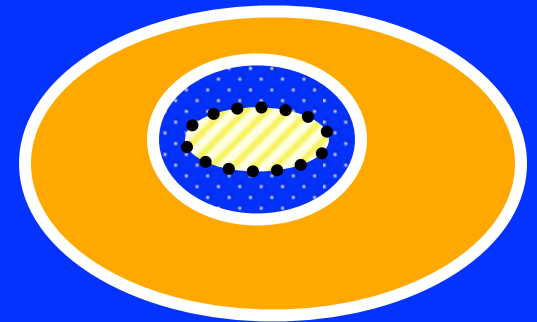
← Micro-organism



Adherence



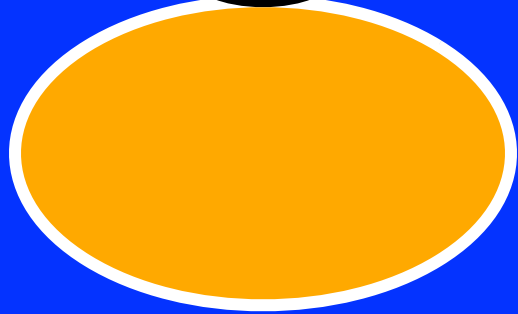
Phagocytosis



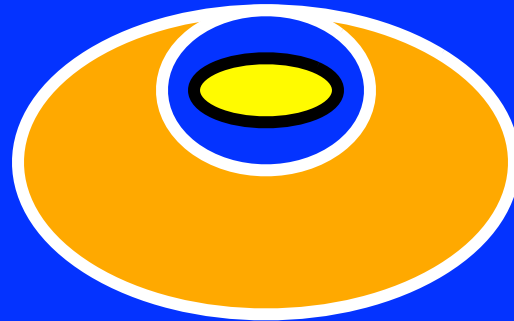
Migration

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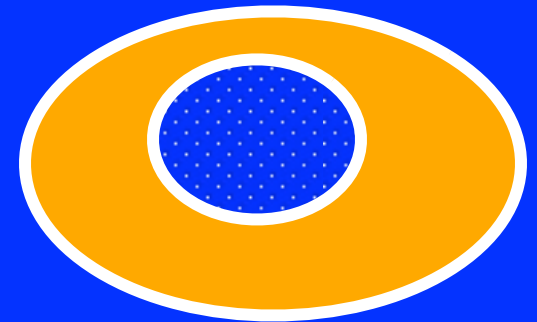
← Micro-organism



Adherence



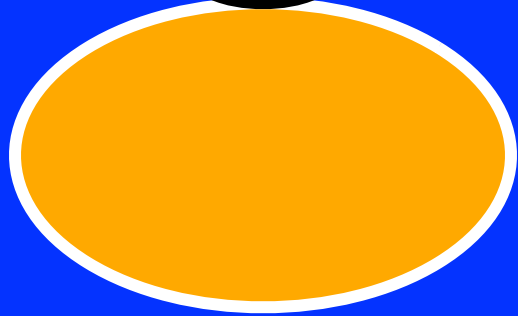
Phagocytosis



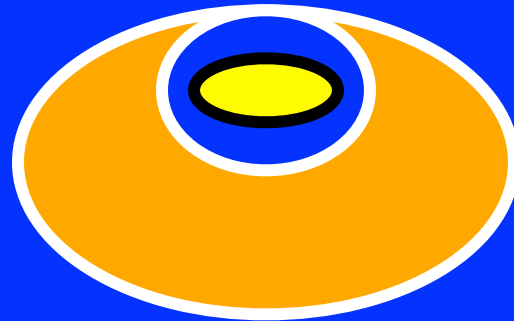
Migration

Phagocytes

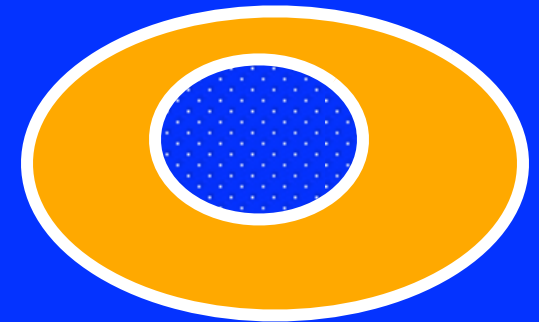
← Micro-organism



Adherence



Phagocytosis



Killing

Migration

Non-specific, cellular immunity

- Problems if:
Neutropoenia, deficient adhesion,
chemotaxis or killing
- Staphylococcal or fungal infections

Treatment:

Antibiotics, antifungals,(BMT)

Non-specific, humoral immunity

Complement

- Helps adherence (C3b)
- Biologically active (C3a, C5a)
- Membrane Attack Complex

Acute Phase Proteins (eg CRP)

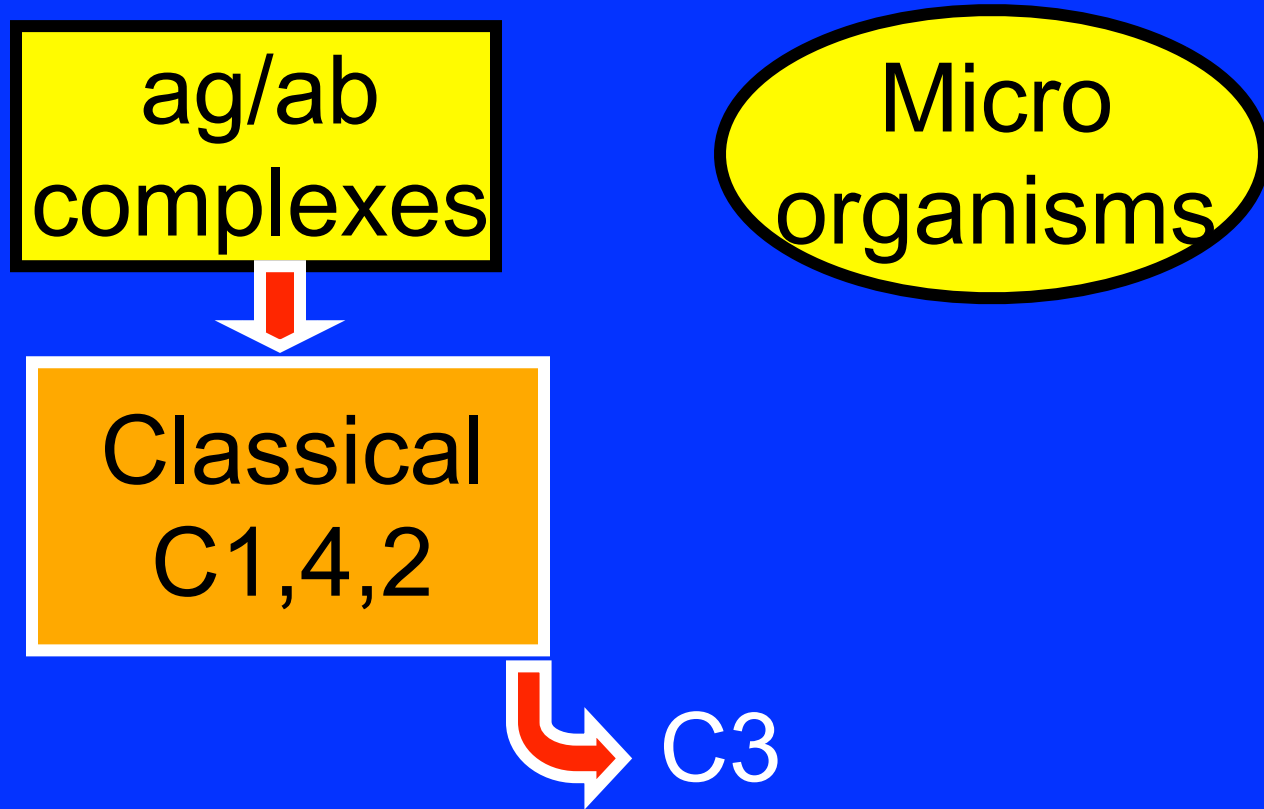
- Bind to organisms, helps C3b adherence

Complement cascade

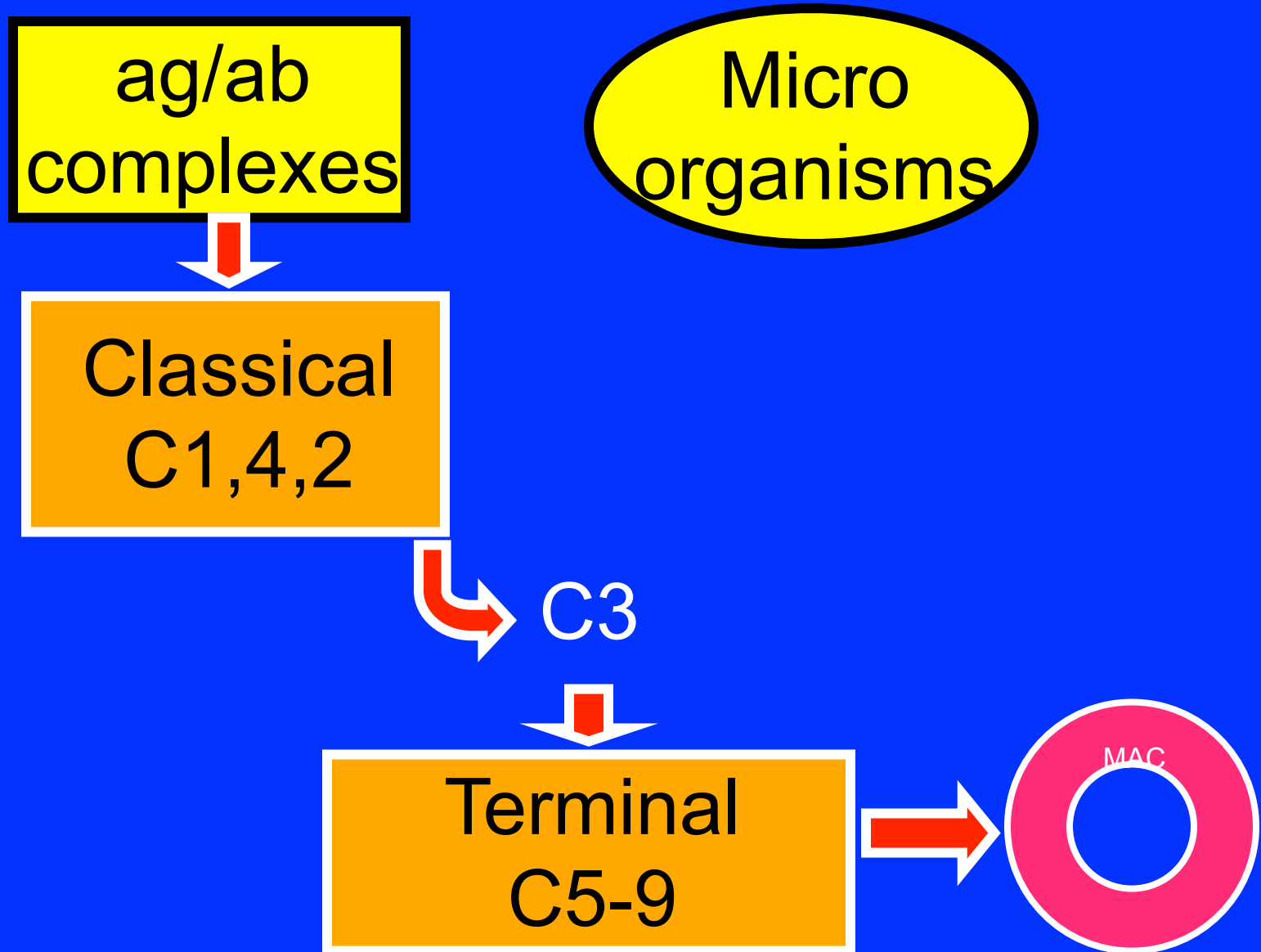
ag/ab
complexes

Micro
organisms

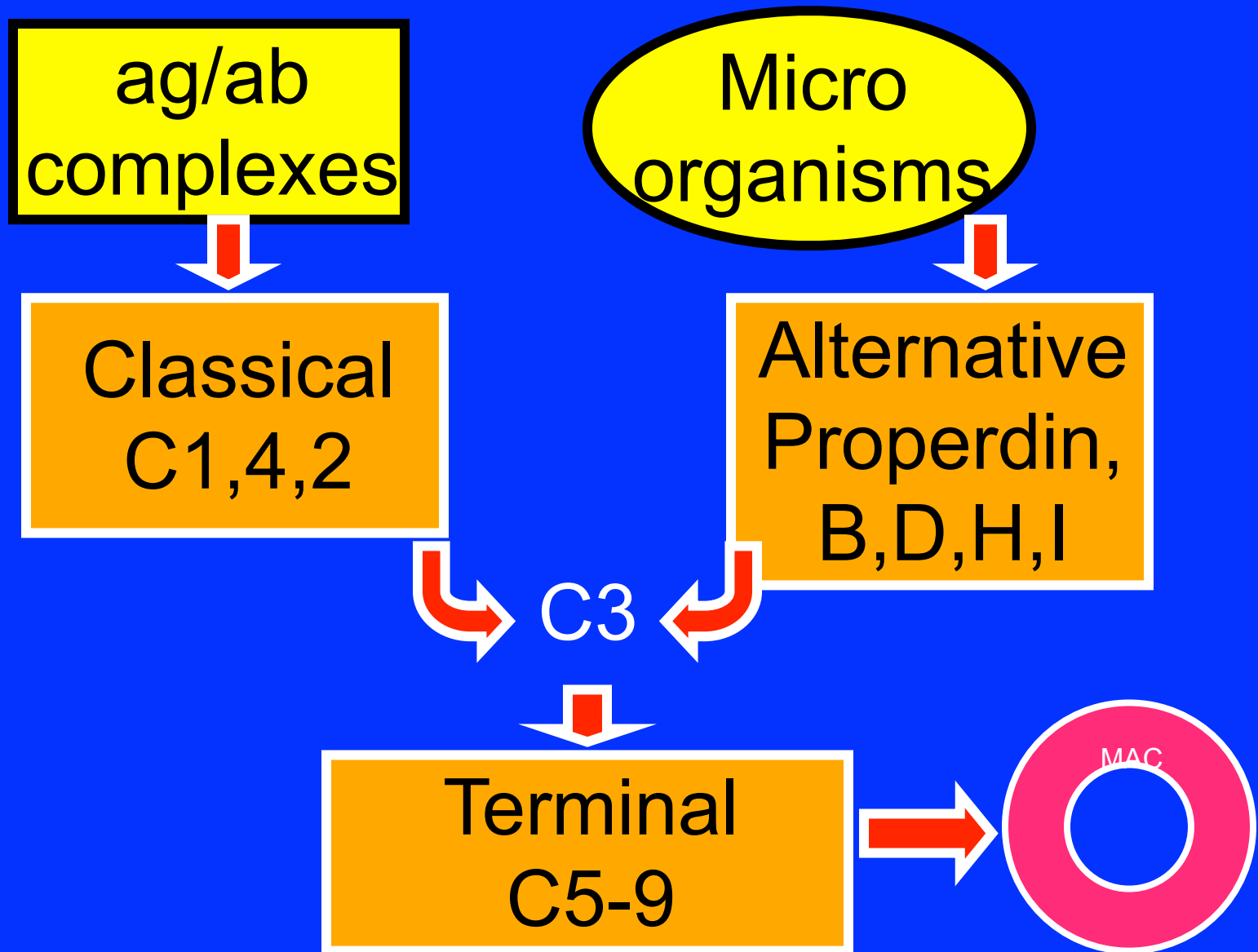
Complement cascade



Complement cascade



Complement cascade



Non-specific, humoral immunity

- Problems if:
deficient complement components
- Early - vasculitis
Late - sepsis (meningo/ pneumo)

Treatment

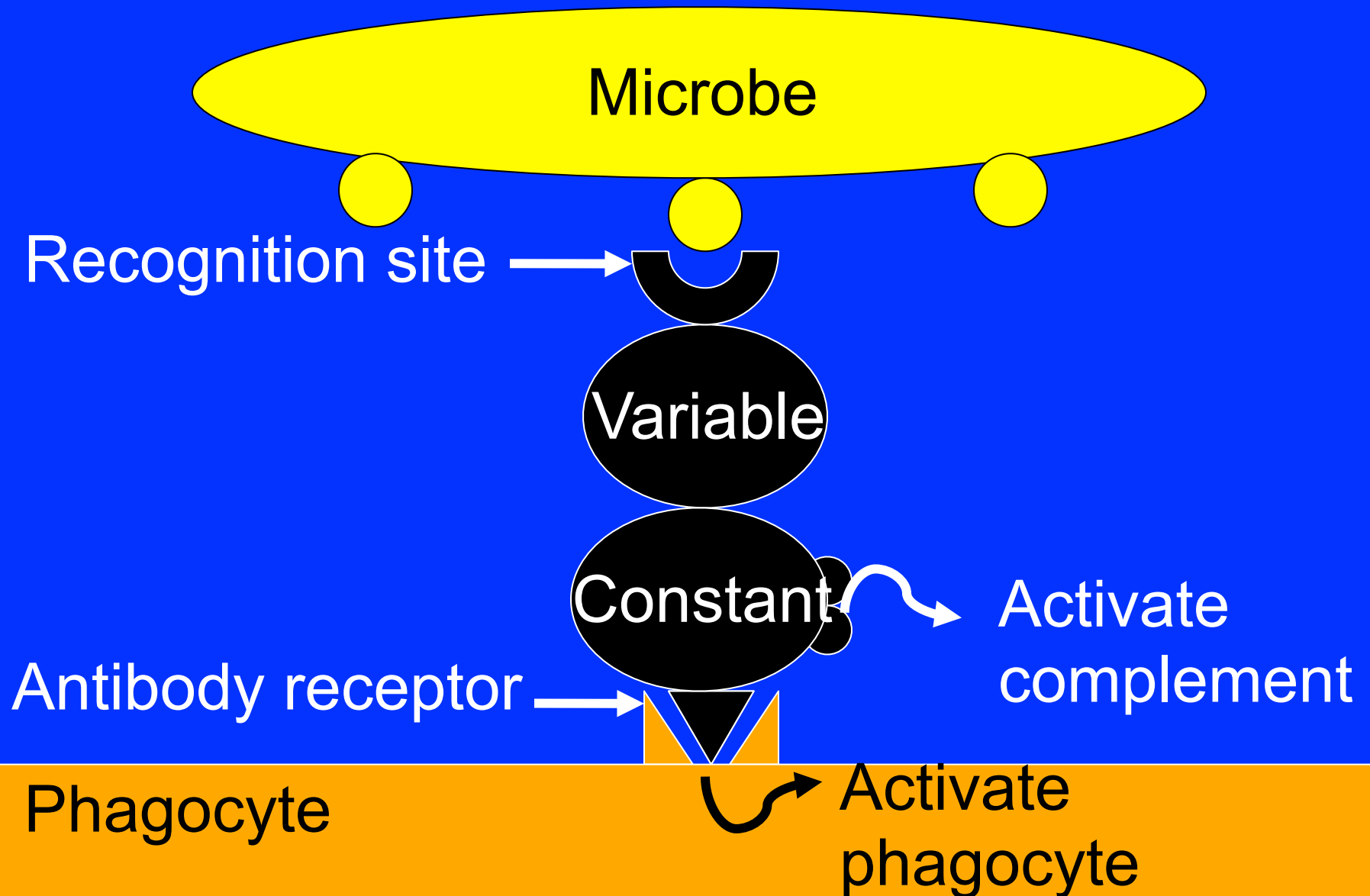
Vaccine, Antibiotics

Specific, humoral immunity

Organisms may avoid complement or prevent cell activation. Thus need a **SPECIFIC** response, which can:

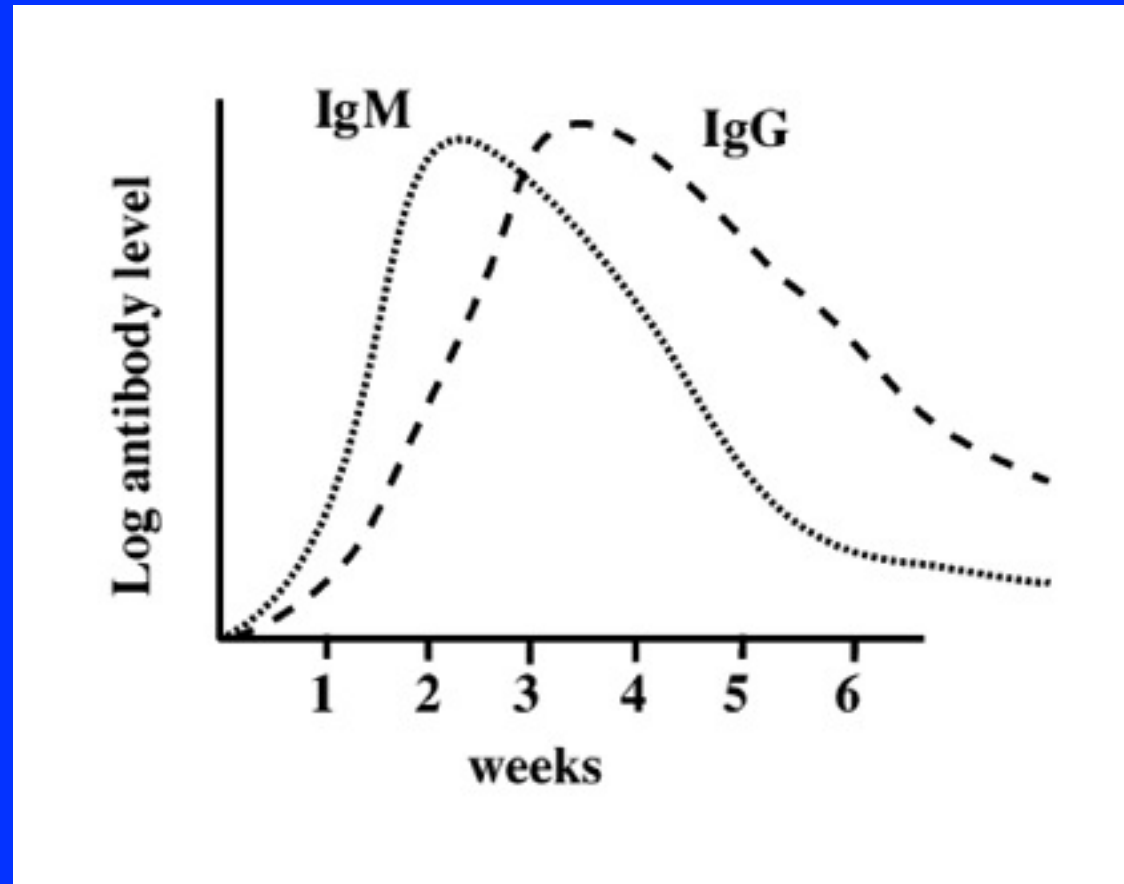
- Stick to the microbe
- Activate complement
- Stimulate phagocytosis

The antibody molecule



Antibody

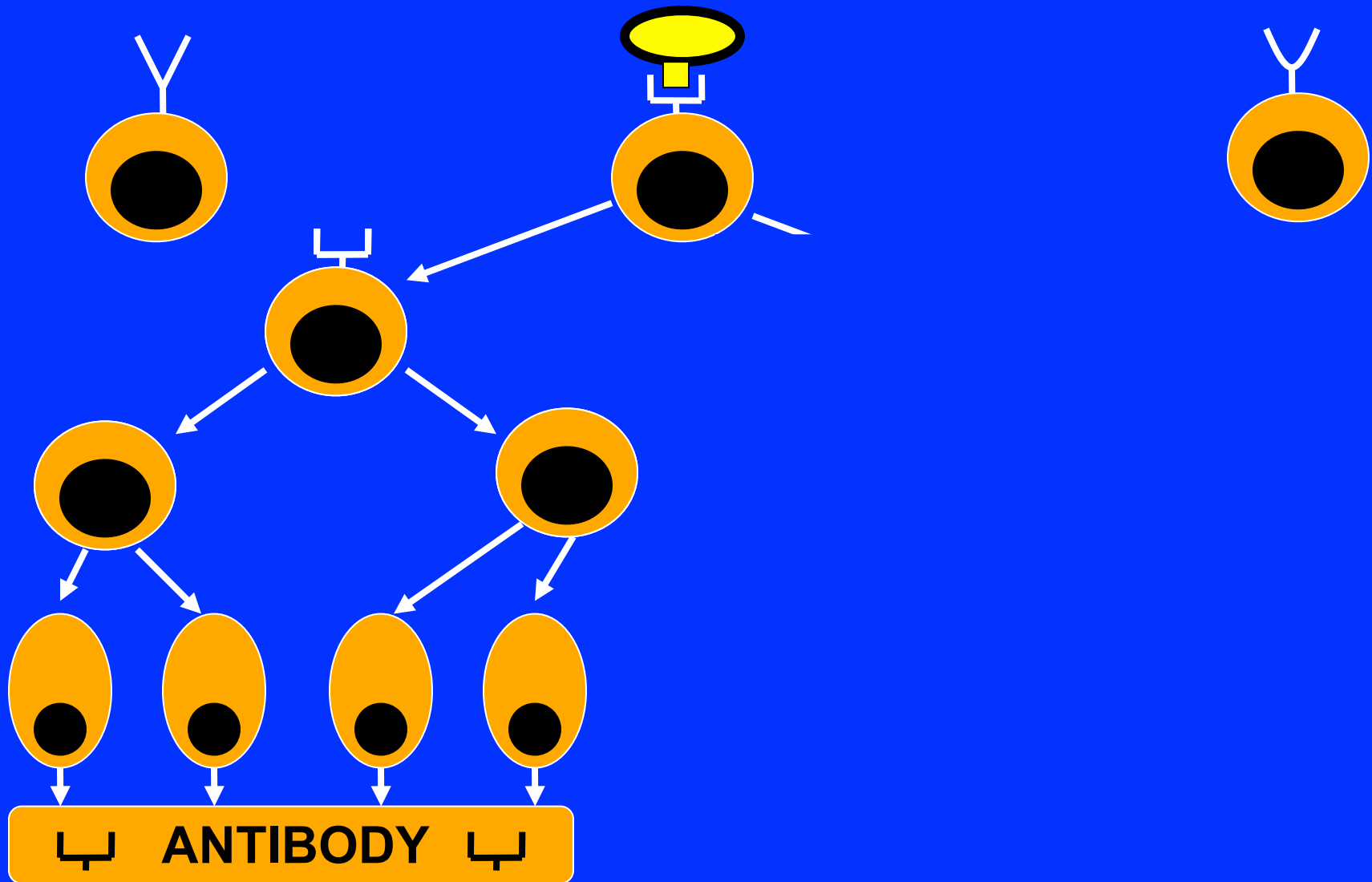
- Specific protection against infection
- IgM produced early, short lived
- IgG produced later, lasts longer
- IgA protects mucosal surfaces



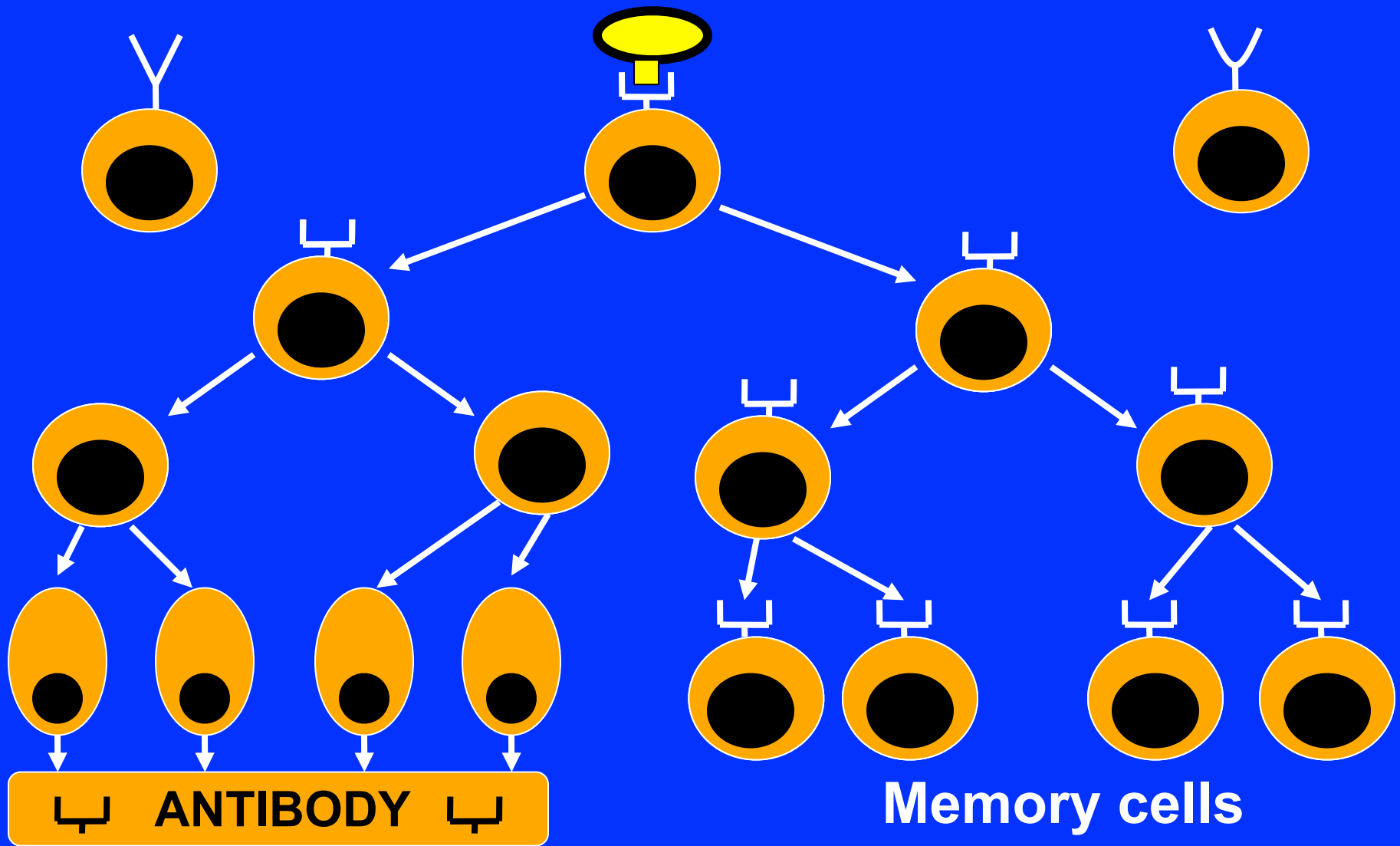
B cells

- Each B cells makes a specific antibody. Preformed & expressed on the surface.
- When it meets the correct antigen, this clone proliferates to make antibody & memory cells. Takes a few days.
- Next response to that specific antigen, more rapid, more antibody and more effective.

Lymphocyte selective activation, clonal expansion and maturation of B cells.



Lymphocyte selective activation, clonal expansion and maturation of B cells.



Specific, humoral immunity

- Problems if
Deficient B cells or antibody
- Pyogenic bacteria

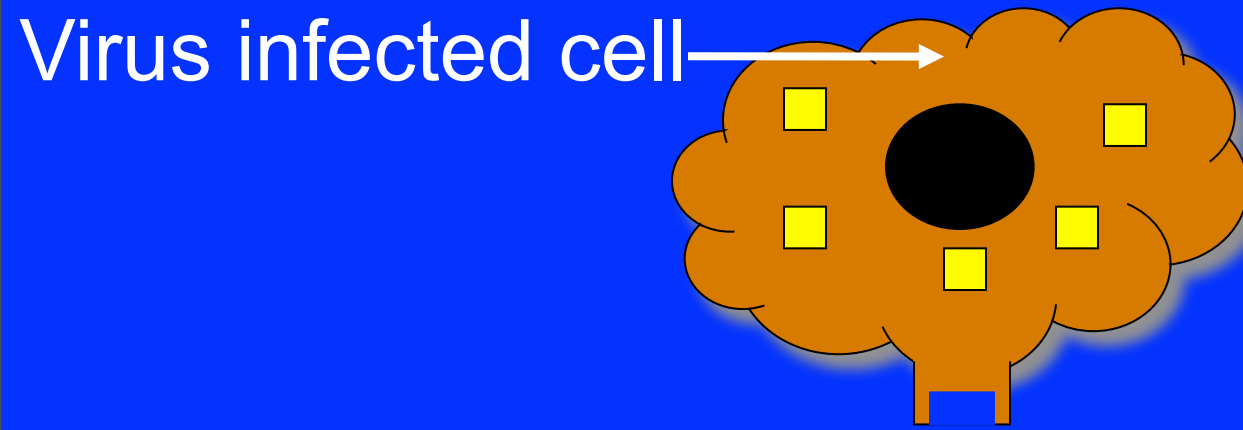
Treatment

Immunoglobulin

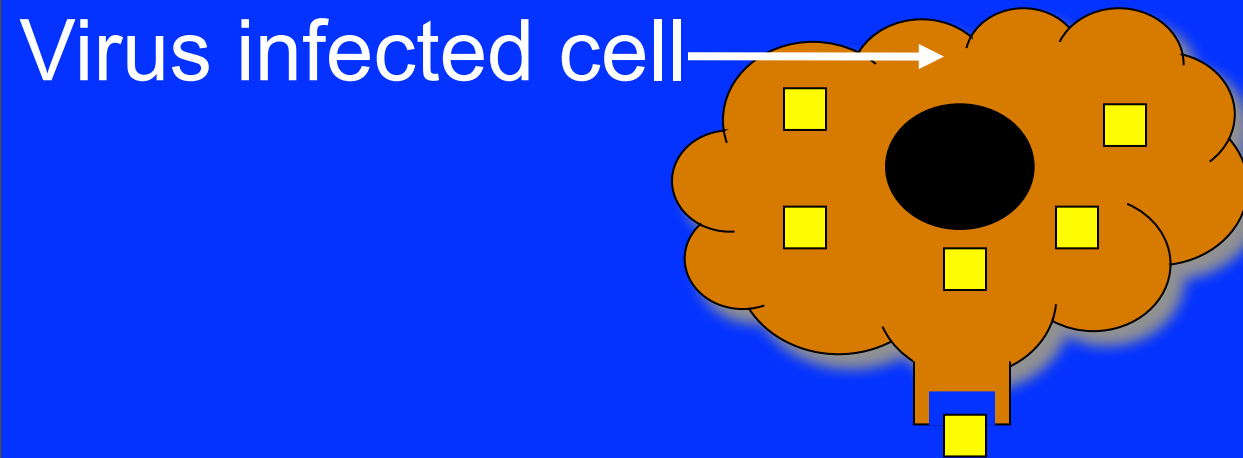
Specific, cellular immunity

- Organisms may “hide” in cells
- Need to recognise cells (MHC) and the SPECIFIC antigen

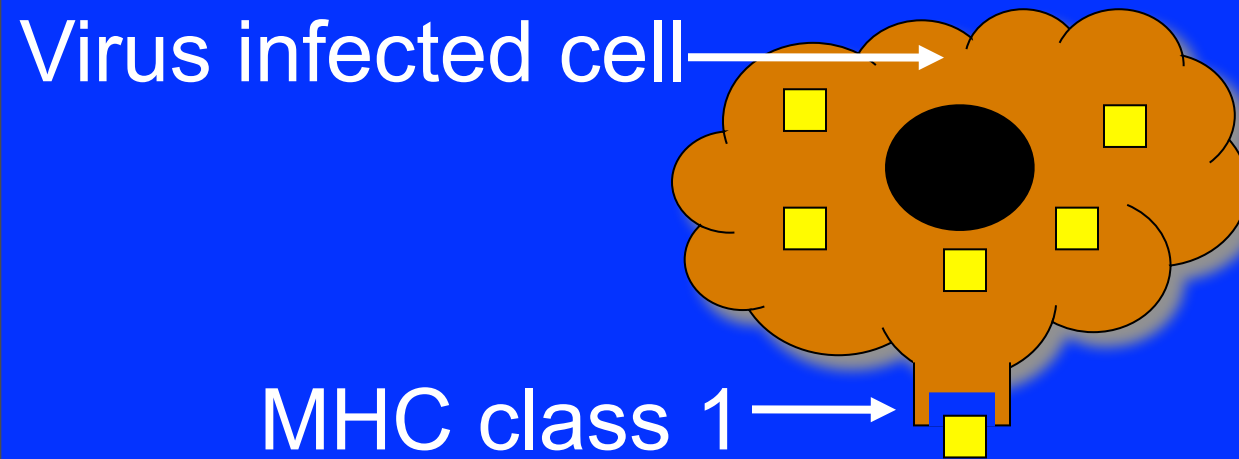
Cytotoxic T cell



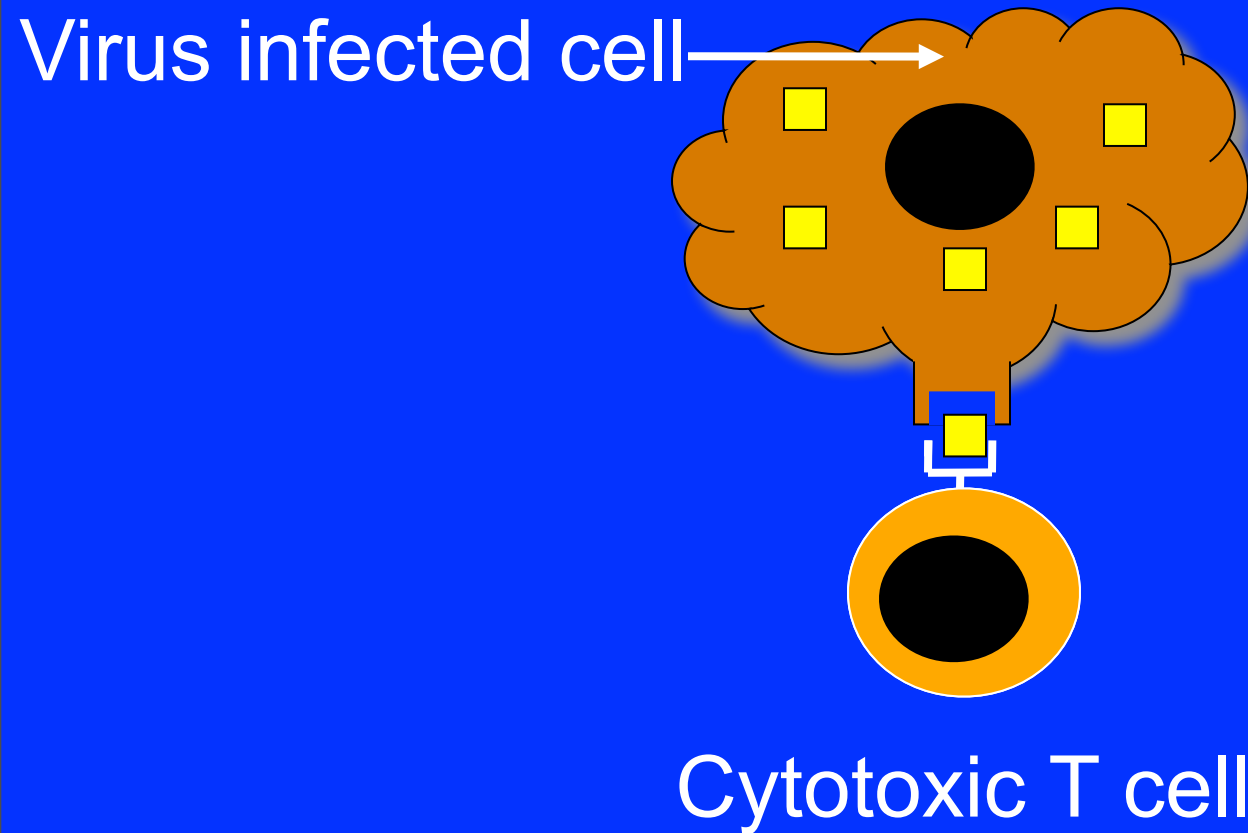
Cytotoxic T cell



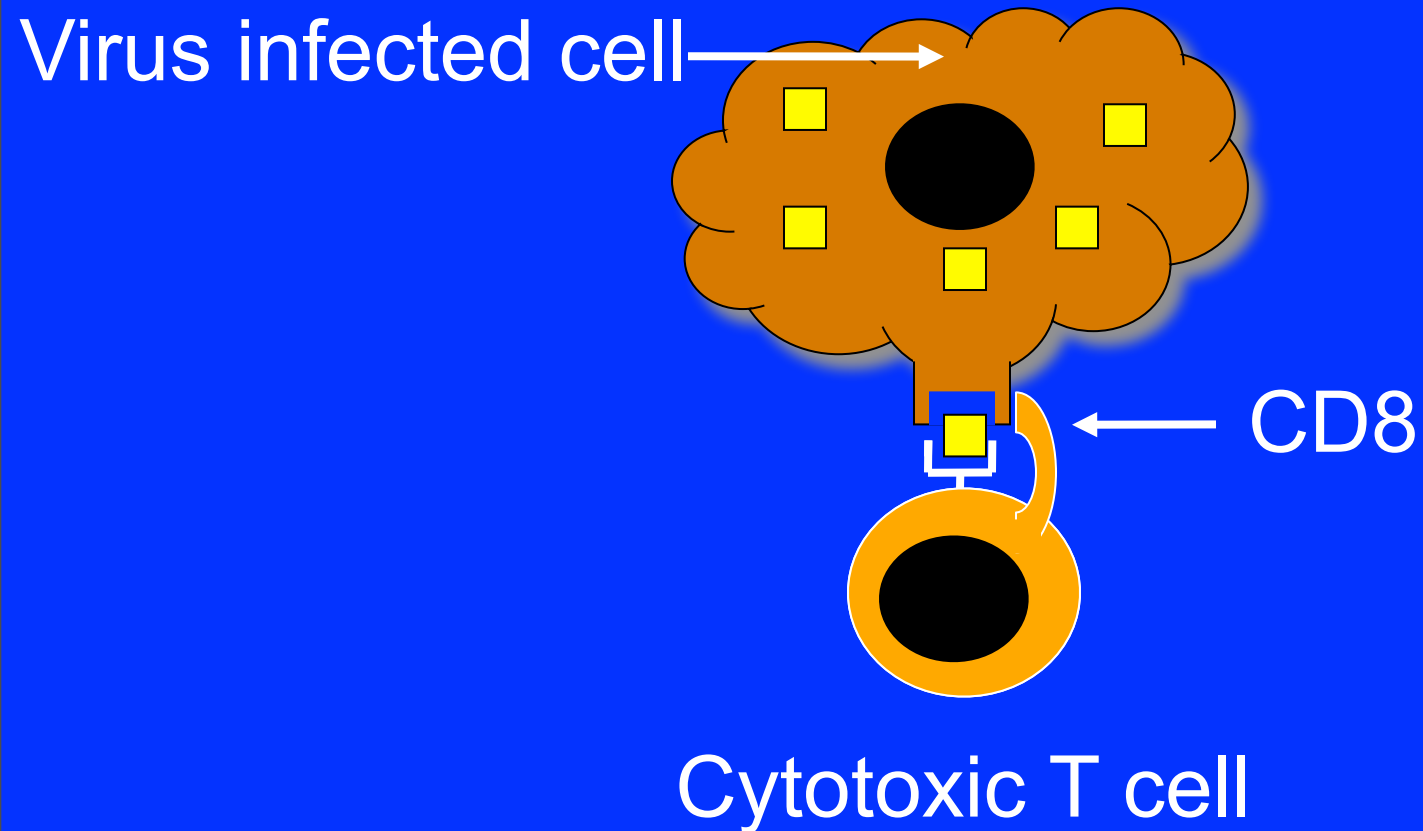
Cytotoxic T cell



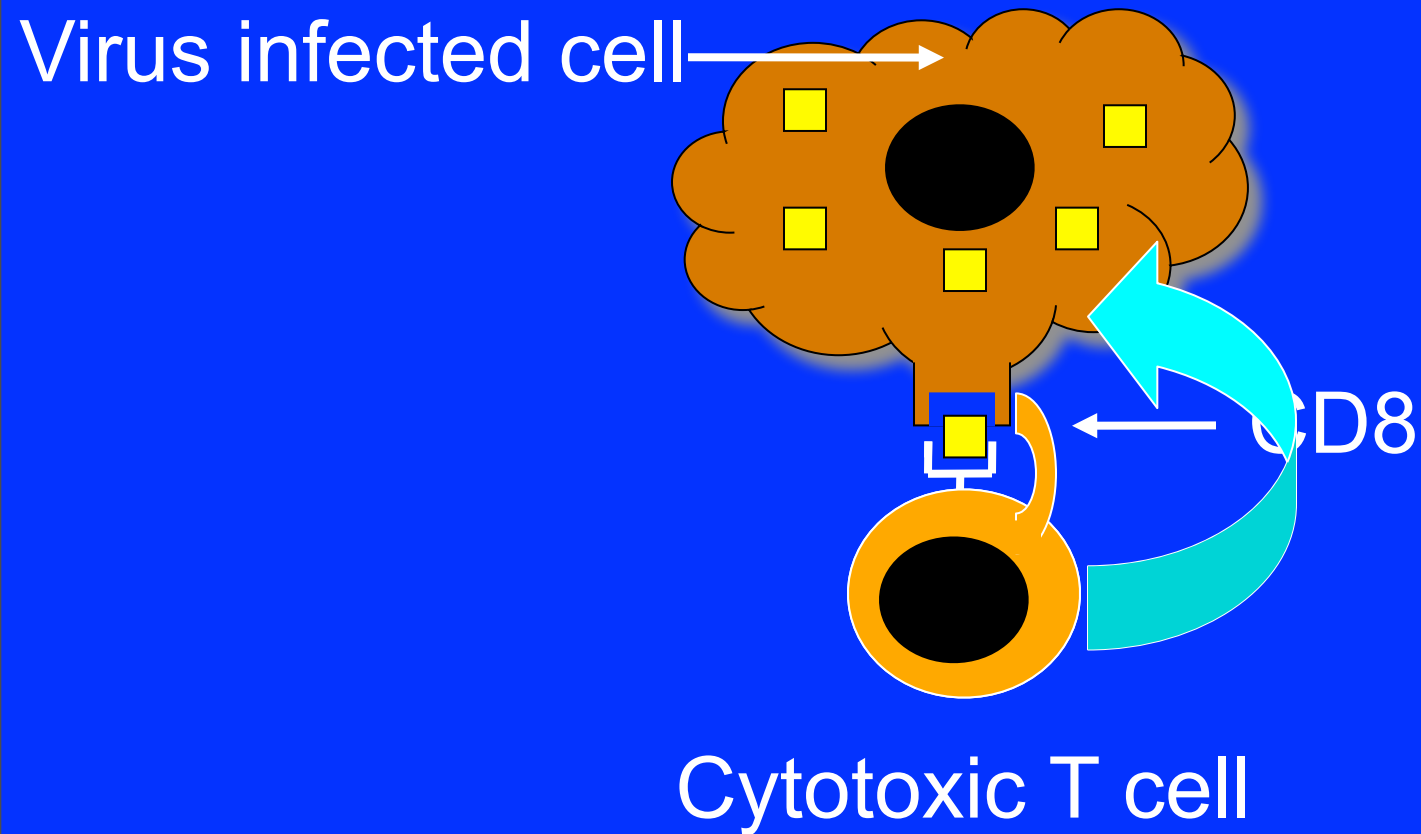
Cytotoxic T cell



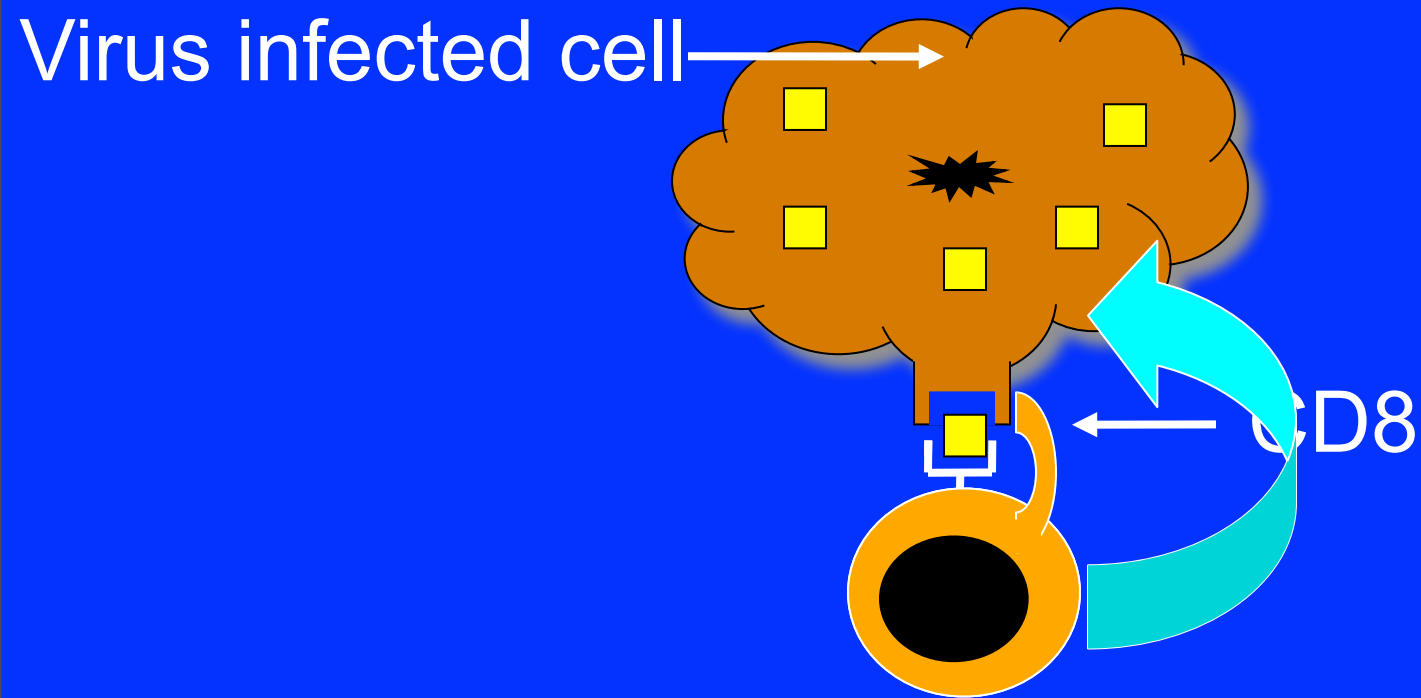
Cytotoxic T cell



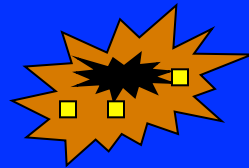
Cytotoxic T cell



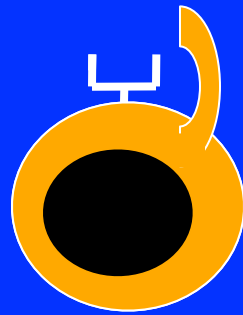
Cytotoxic T cell



Cytotoxic T cell



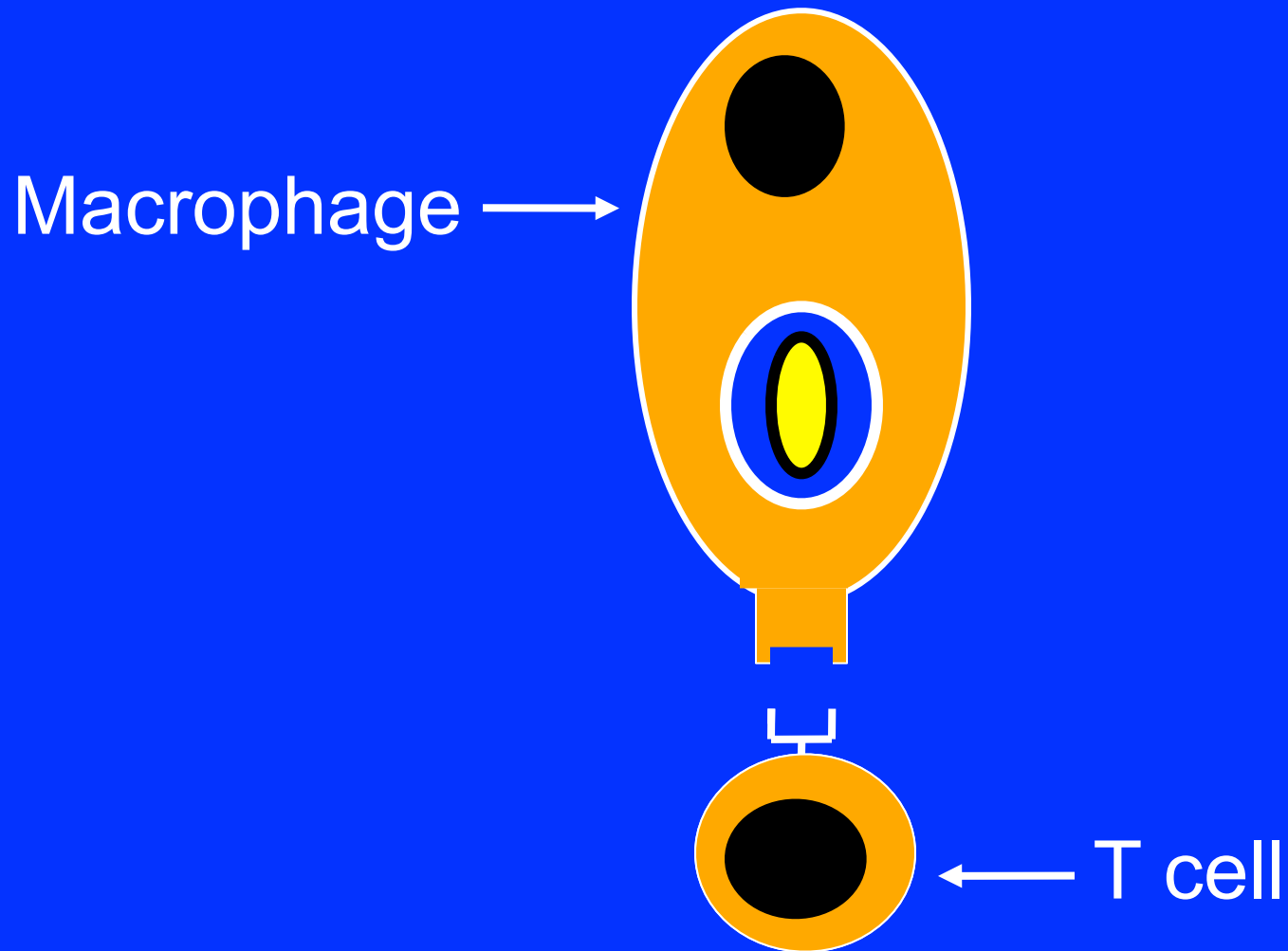
Apoptosis



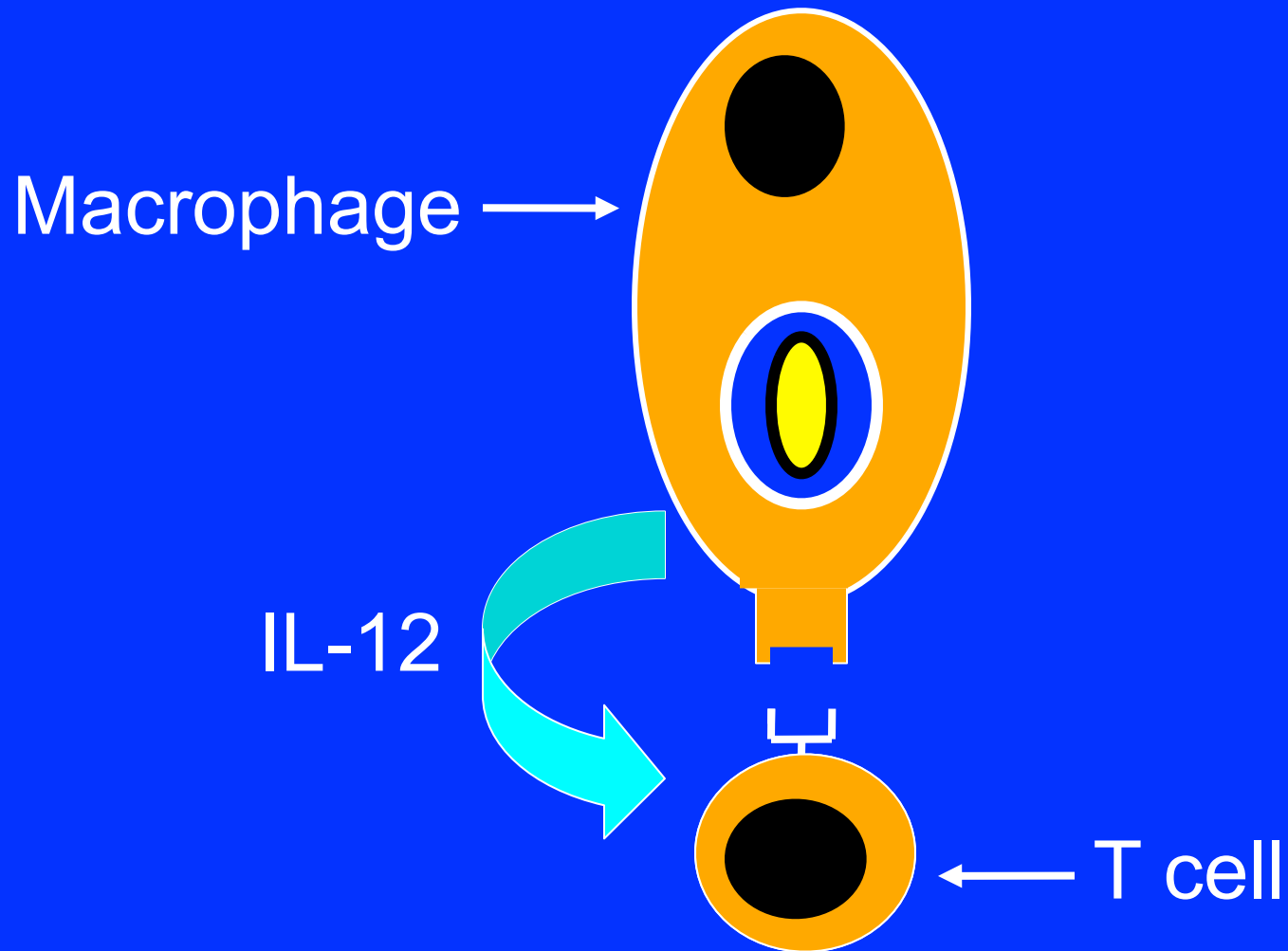
T cells

- Cytotoxic to cells infected with viruses
- Produce lymphokines to activate macrophages to kill ingested organisms

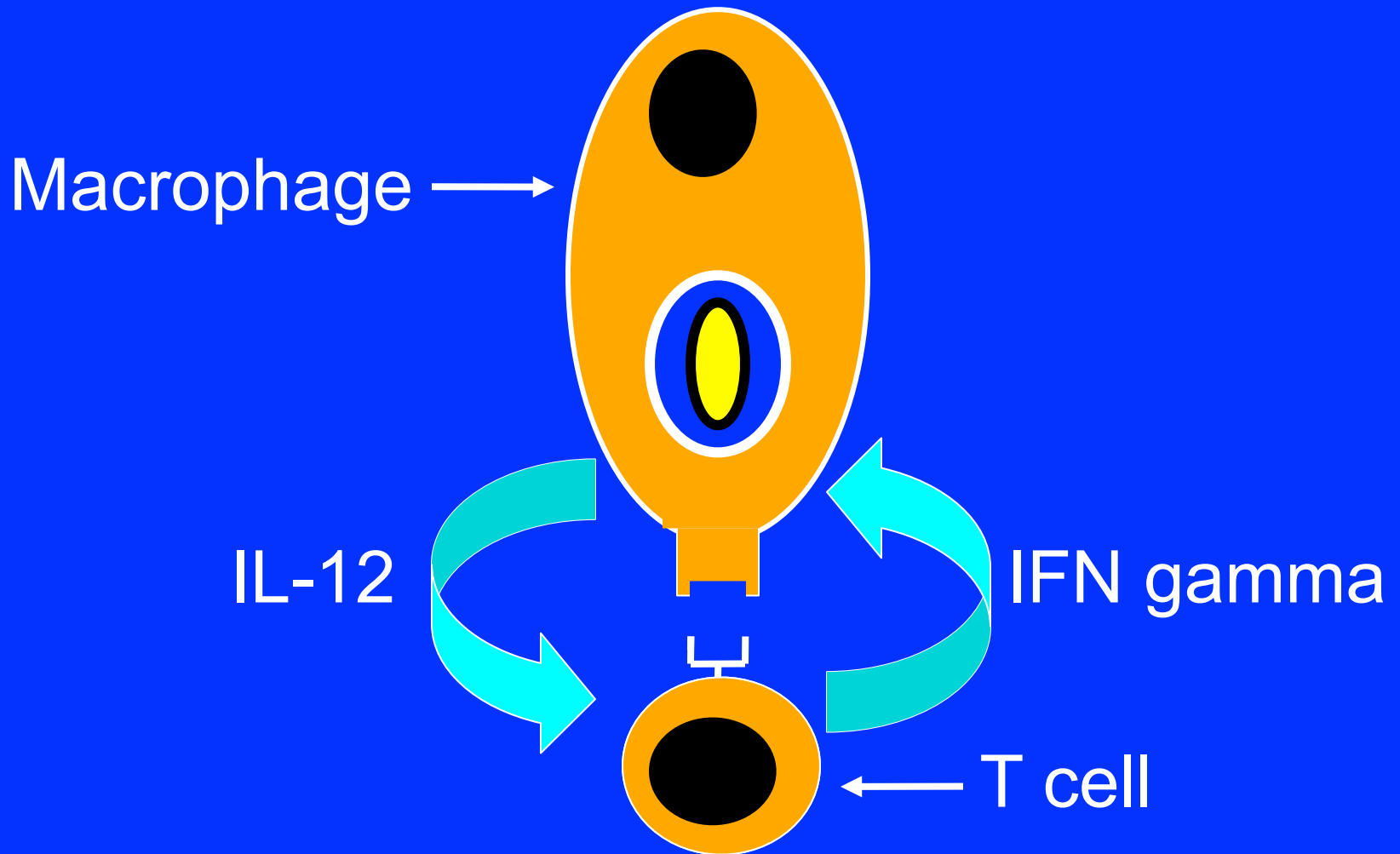
Macrophage activation



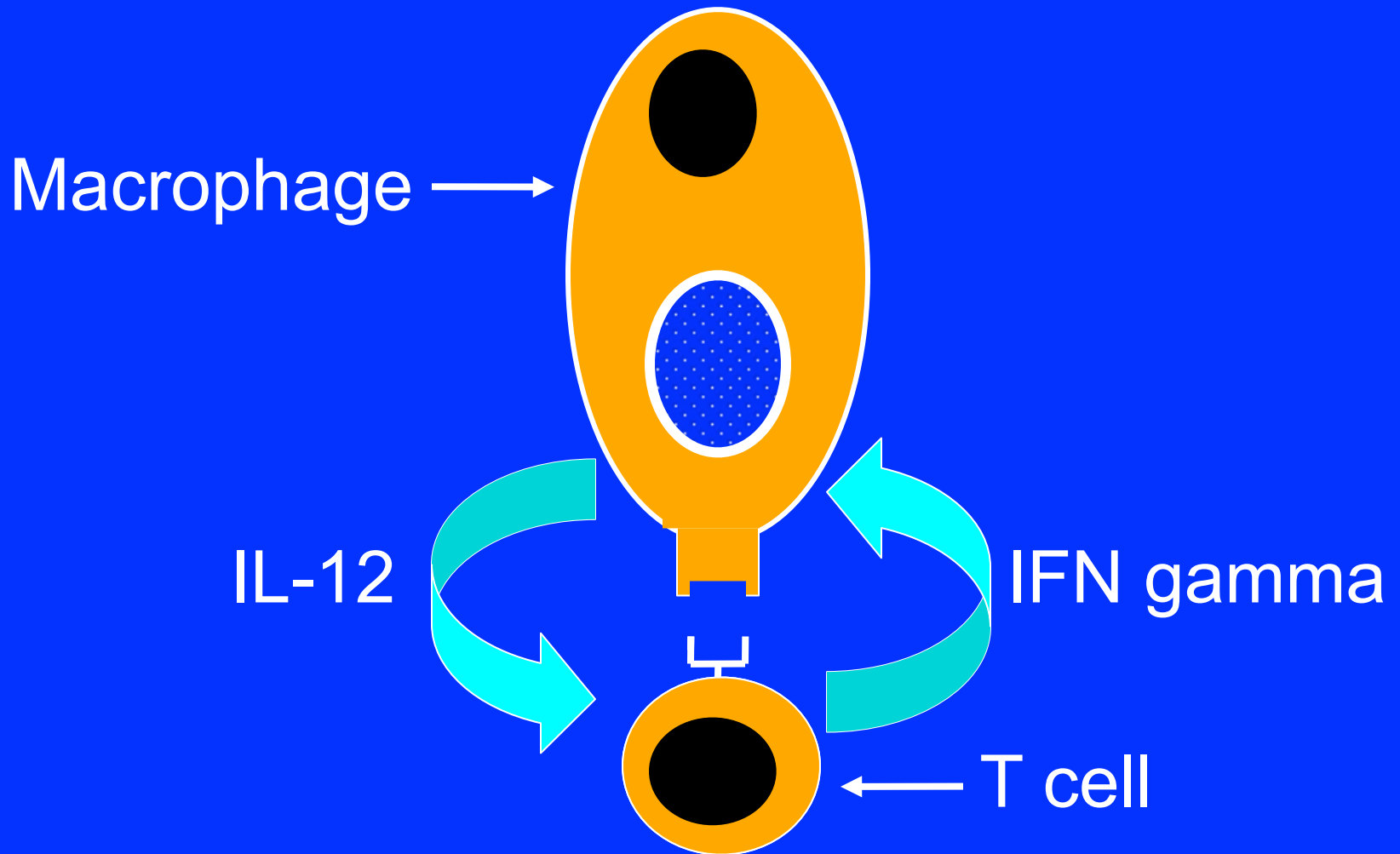
Macrophage activation



Macrophage activation



Macrophage activation



Specific, cellular immunity

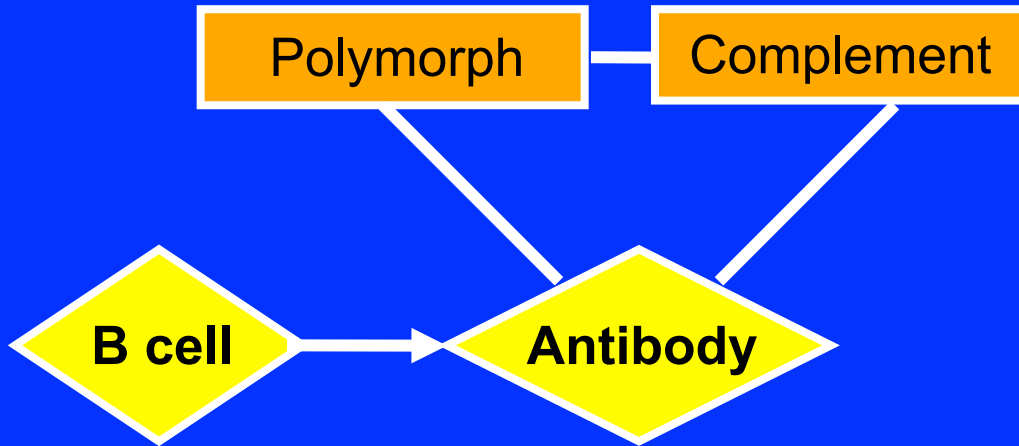
- Problems if:
Deficient T cells or poor cell signalling
- Viral, fungal, intracellular bacterial infections

Treatment

Antibiotics (Septrin), BMT

The Immune System

Non-specific and Specific

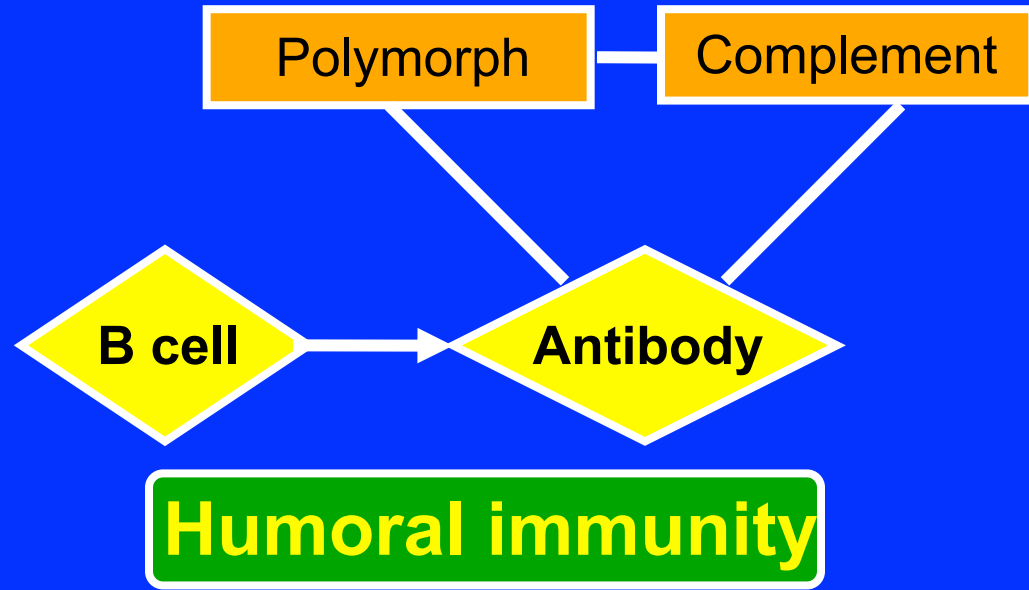


The Immune System

Non-specific

and

Specific

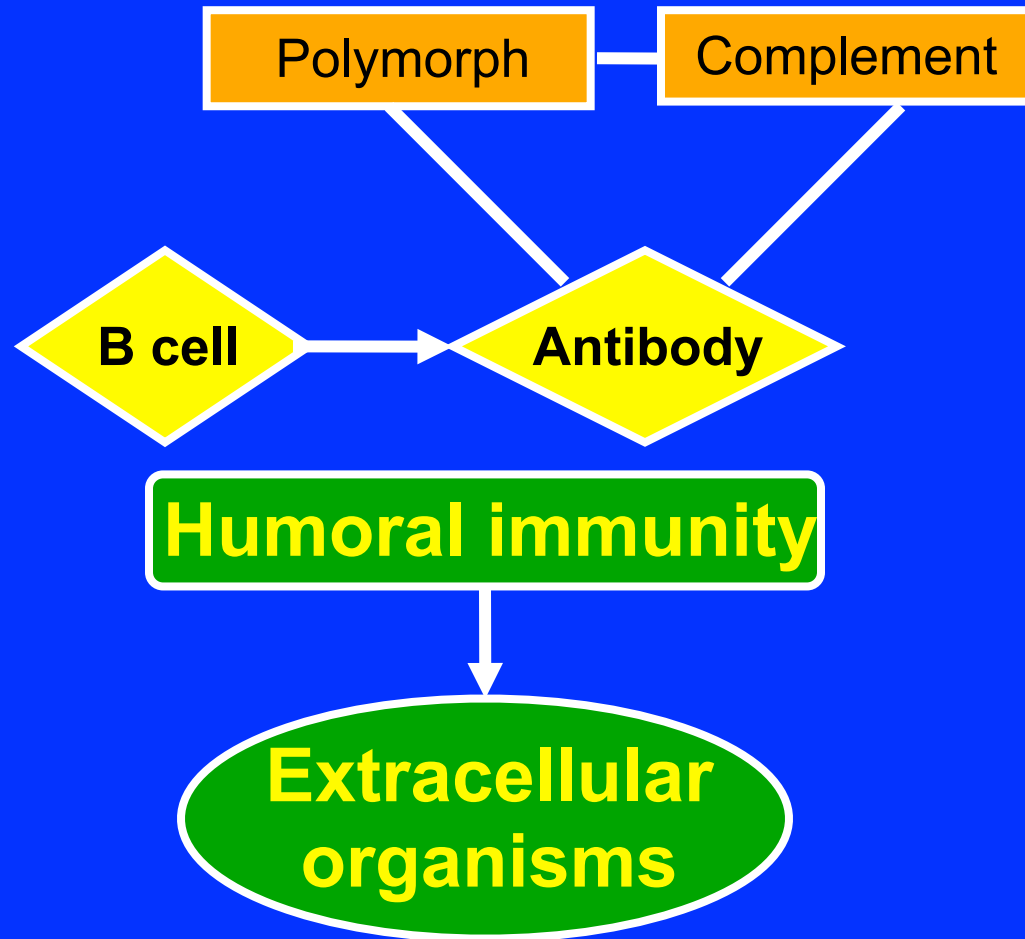


The Immune System

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Specific

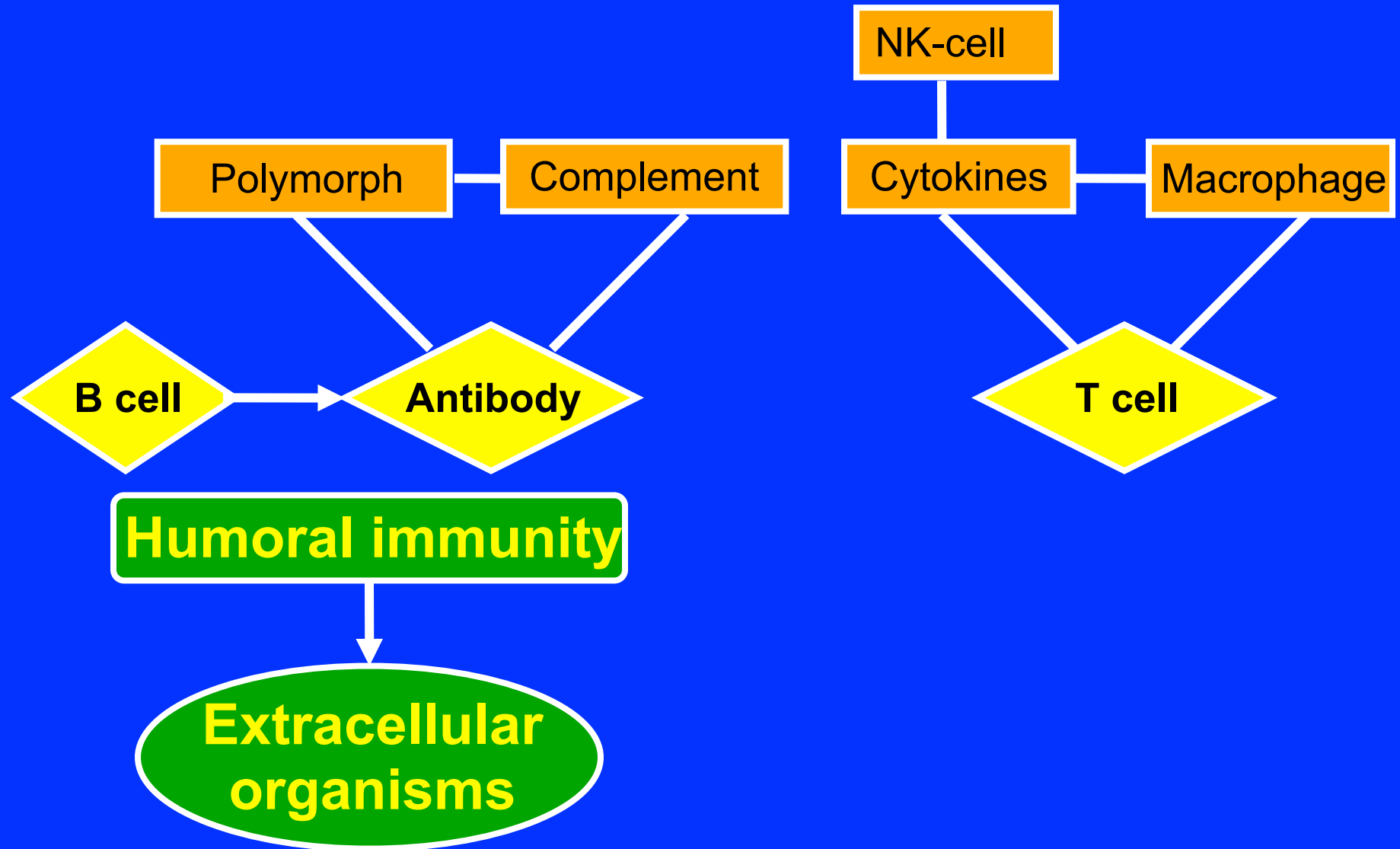


The Immune System

Non-specific

and

Specific

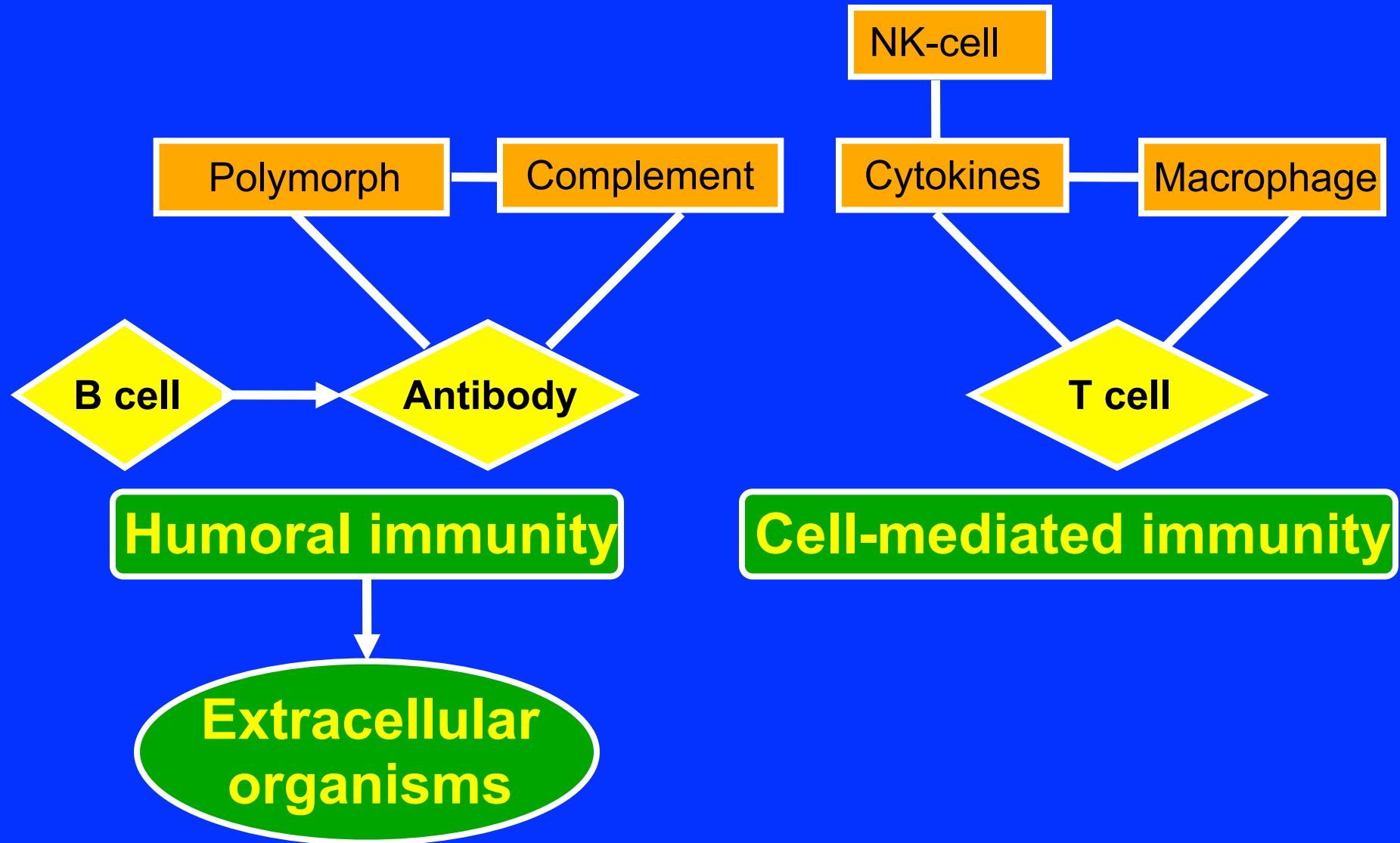


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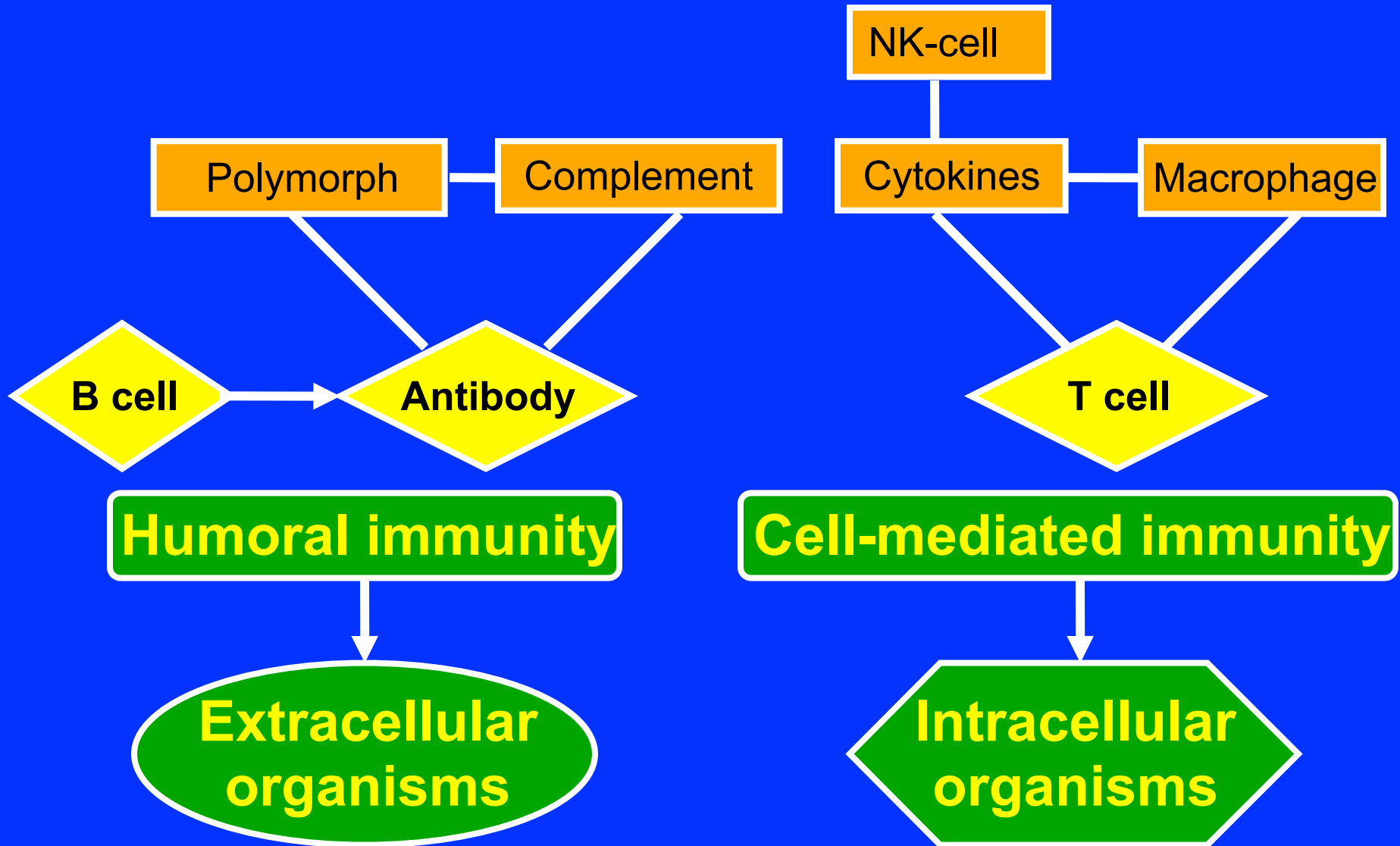


The Immune System

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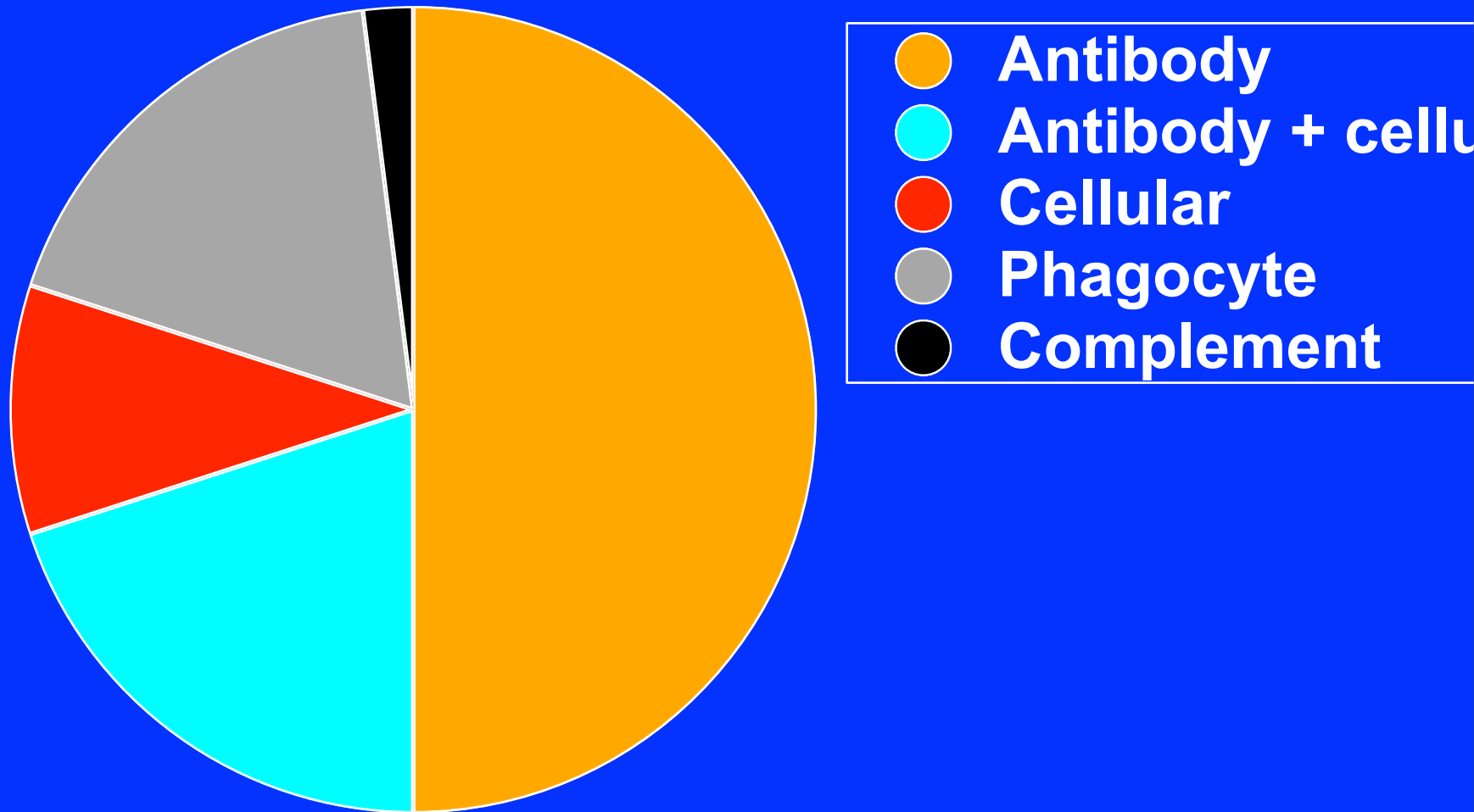


The Immune system IS there
as a defence against infection.

Immunodeficiencies

- Primary Immunodeficiencies are not common 1:10,000
- Secondary Immunodeficiencies are commoner; prematurity, malnutrition, Haem/Onc, transplants, steroids, HIV
- Susceptibility to infection depends on which part(s) of the immune system are affected

Primary Immunodeficiencies



Clues to immunodeficiency;

Severe infections

- disseminated chickenpox

Prolonged infections

- chickenpox for >1 week

Unusual infections

- pneumocystis pneumonia

Recurrent common infections

10 warning signs of primary immunodeficiency

www.info4pi.org

1. 4 new ear infections within 1 year;
2. 2 serious sinus infections within 1 year;
3. 2 months of oral antibiotic treatment with little effect;
4. 2 episodes of pneumonia within 1 year;
5. failure of an infant to gain weight or grow normally;
6. recurrent, deep skin or organ abscesses;
7. persistent thrush in mouth or fungal infection on skin;
8. need for intravenous antibiotics to clear infections;
9. 2 deep-seated infections, including septicaemia;
10. a family history of PID.

Immunologic screening of children with recurrent otitis media.

Immunologists

- Up to 98% of patients with antibody deficiency have otitis, sinusitis, bronchitis
- Many have established bronchiectasis when diagnosed

Immunologic screening of children with recurrent otitis media.

Immunologists

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Non-Specialist

- 5% to 10% of infants and toddlers suffer ≥ 4 episodes of otitis/ year.
- Antibody deficiency is rare among these patients.
- IgA, IgG2 or specific antibody deficiency may occur

Case 1 – born 1997

1998 ottorhoea

2000 Ts&As+grommets
ottorhoea

2001 grommets
ottorhoea

2003 grommets
ottorhoea

2007 grommets
ottorhoea

Case 1 – born 1997

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ottorhoea

2007 grommets
ottorhoea

1999 “recurrent LRTI”

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2007 grommets
ottorhoea

1999 “recurrent LRTI”

2002 “recurrent LRTI”

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otorrhoea

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1999 “recurrent LRTI”

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2009 R pneumonia

Case 1 – born 1997

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otorrhoea

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2006 L pneumonia

2009 R pneumonia



Case 1 – aged 12

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- Chronic suppurative otitis media since 19 months of age

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- Two episodes of pneumonia – previous “chest infections”

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Case 1 – aged 12

- Chronic suppurative otitis media since 19 months of age
- Two episodes of pneumonia – previous “chest infections”
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Could this child have immune deficiency?

Investigations

Investigations

FBC:

Hb 12

WBC 8.1 (N 4.3, L 2.4)

Plts 275

Investigations

FBC:

Hb 12

WBC 8.1 (N 4.3, L 2.4)

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Investigations

FBC:

Hb 12

WBC 8.1 (N 4.3, L 2.4)

Plts 275

Immunoglobulins

Investigations

FBC:

Hb 12

WBC 8.1 (N 4.3, L 2.4)

Plts 275

Immunoglobulins

IgG <1.1 (7.4-14)

Investigations

FBC:

Hb 12

WBC 8.1 (N 4.3, L 2.4)

Plts 275

Immunoglobulins

IgG <1.1 (7.4-14)

IgA <0.05 (0.6-3.3)

Investigations

FBC:

Hb 12

WBC 8.1 (N 4.3, L 2.4)

Plts 275

Immunoglobulins

IgG <1.1 (7.4-14)

IgA <0.05 (0.6-3.3)

IgM 8.26 (0.5-2.3)

Investigations

FBC:

Hb 12

WBC 8.1 (N 4.3, L 2.4)

Plts 275

Immunoglobulins

IgG <1.1 (7.4-14)

IgA <0.05 (0.6-3.3)

IgM 8.26 (0.5-2.3)

- Diagnosis – “Antibody deficiency”
- Treatment – immunoglobulin replacement

Further tests

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If FBC and immunoglobulins normal;

Further tests

If FBC and immunoglobulins normal;
check specific antibodies to:

Further tests

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check specific antibodies to:

Pneumococcal polysaccharide

Further tests

If FBC and immunoglobulins normal;
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Haemophilus influenzae type b (Hib)

Further tests

If FBC and immunoglobulins normal;
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Haemophilus influenzae type b (Hib)

Tetanus

Further tests

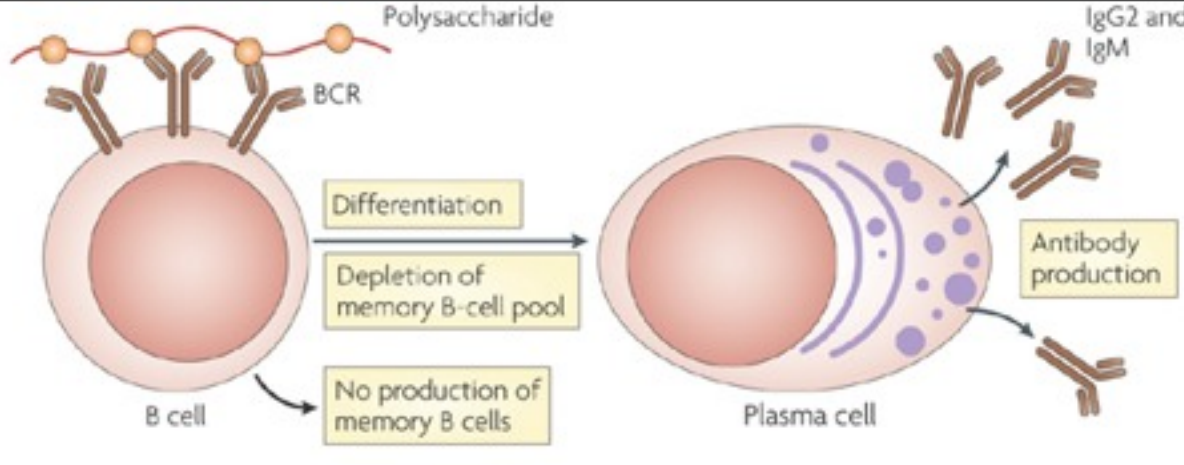
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Tetanus

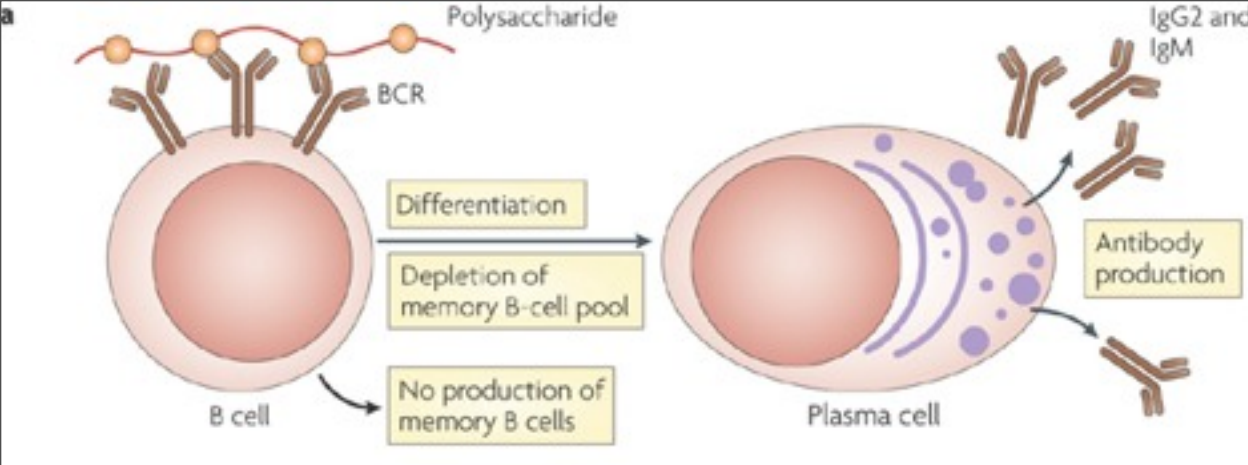
If low, give vaccines and recheck



Response to
polysaccharide

Age >2yrs

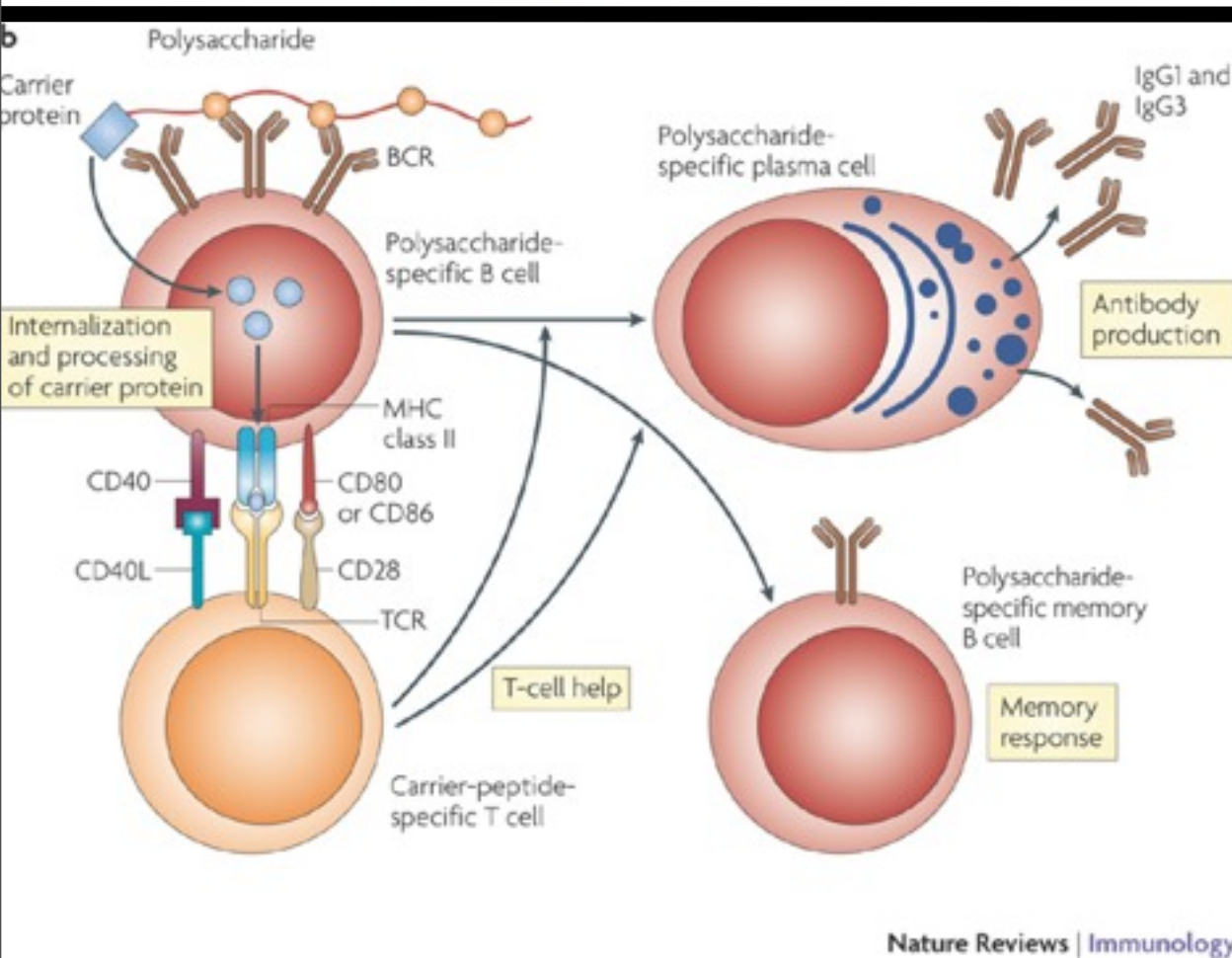
No memory



Response to polysaccharide

Age >2yrs

No memory



Response to protein conjugate

Any age

Memory

Hierarchy of vaccine responses

1. Polysaccharide (pneumovax)
2. Conjugate (Hib)
3. Tetanus

Hierarchy of vaccine responses

Poor response

1. Polysaccharide (pneumovax)
2. Conjugate (Hib)
3. Tetanus

Hierarchy of vaccine responses

Poor response

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Hierarchy of vaccine responses

Poor response

1. Polysaccharide (pneumovax)



2. Conjugate (Hib)



3. Tetanus

Hierarchy of vaccine responses

Poor response

1. Polysaccharide (pneumovax)



2. Conjugate (Hib)



3. Tetanus



The clinical syndrome of specific antibody deficiency in children.

Clin Exp Immunol 2006;146: 486–492

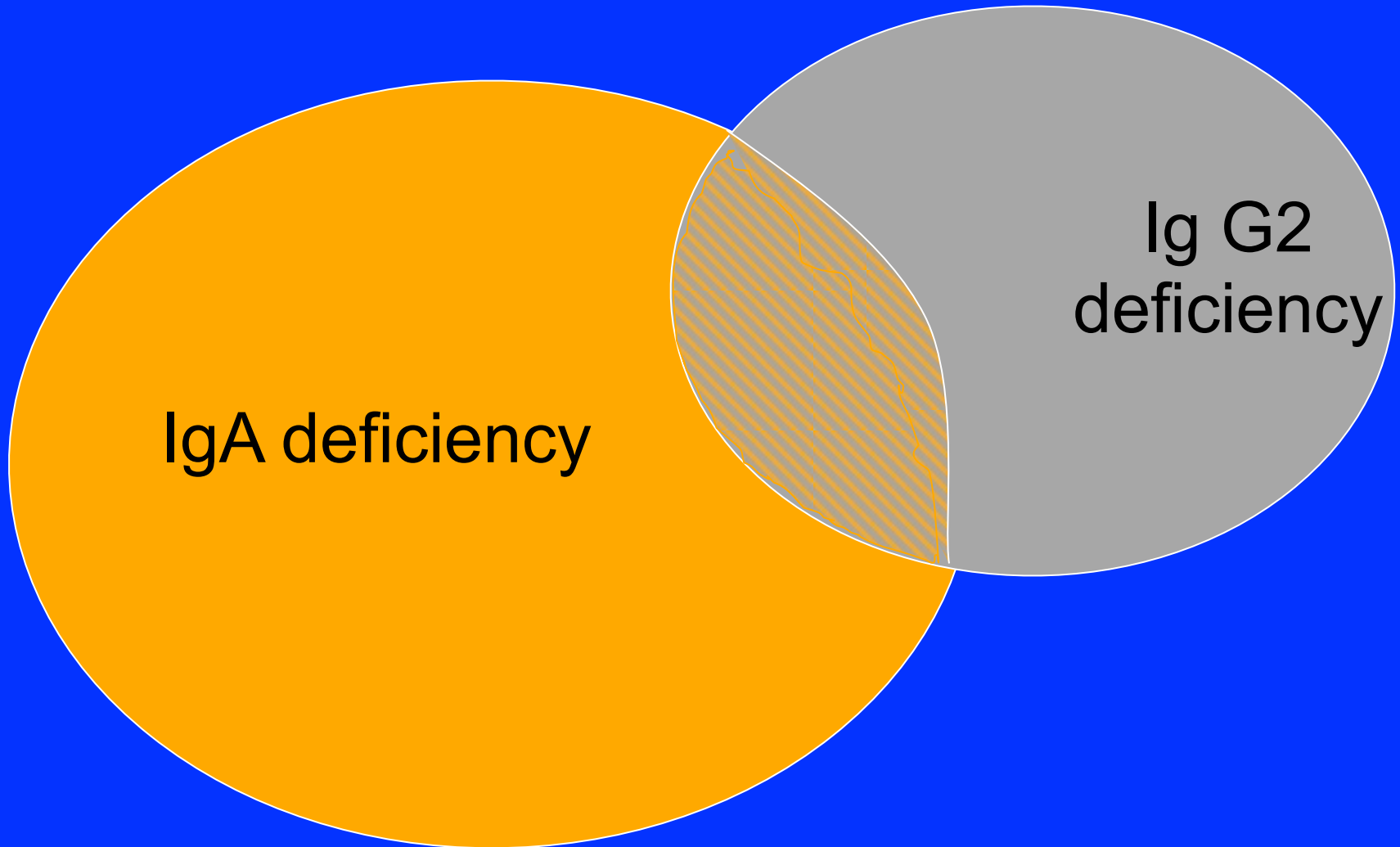
- <4-fold increase in titre following 23-valent unconjugated pneumococcal immunisation (Pneumovax)
- Associated with history of otitis media, particularly in association with chronic otorrhoea (RR 4.64)
- Found in 6–14% of children evaluated for recurrent infection

Overlapping conditions

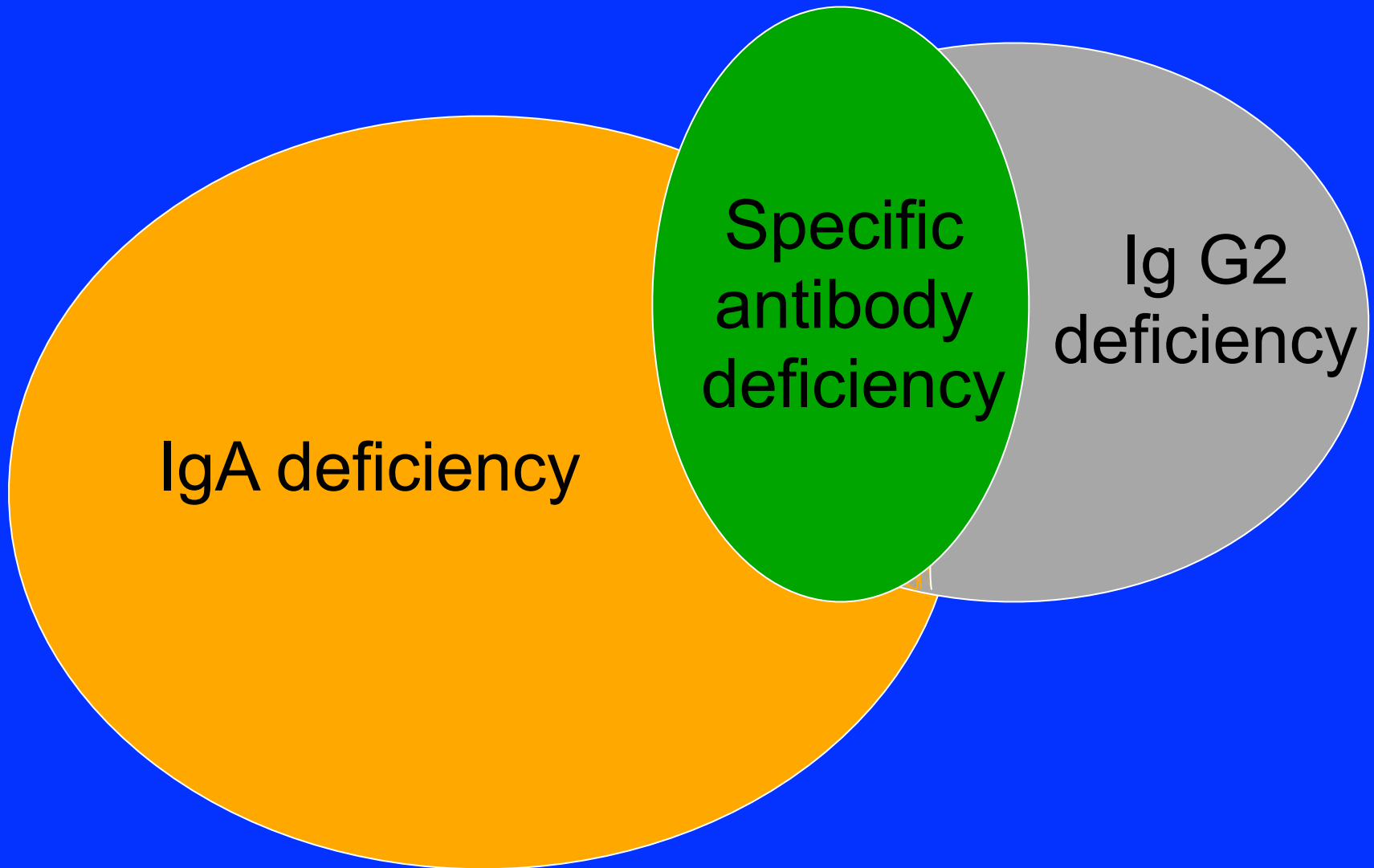


IgA deficiency

Overlapping conditions



Overlapping conditions



Immunologic screening of children with recurrent otitis media.

- Recurrent otitis media with chronic otorrhoea
- Recurrent otitis media with other respiratory infections
- Family History

Immunologic screening of children with recurrent otitis media.

- Recurrent otitis media with chronic otorrhoea
- Recurrent otitis media with other respiratory infections
- Family History

FBC

Immunoglobulins (Ig G, Ig A, Ig M)

Specific Antibody responses (Pneumo, Hib, Tet)

The Immune system is NOT there;

- To baffle medical students
- To keep Immunologists in a job
- To encourage experiments on mice

The Immune system IS there
as a defence against infection.

If you think it is not working

SEEK ADVICE