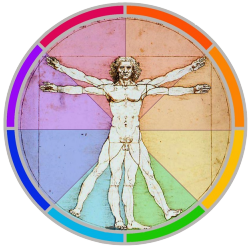
HUBS191 Lecture Material

This pre-lecture material is to help you prepare for the lecture and to assist your note-taking within the lecture, it is NOT a substitute for the lecture !



Please note that although every effort is made to ensure this pre-lecture material corresponds to the live-lecture there may be differences / additions.

HUBS 191
Lecture 32

Innate Immunity II

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University of Otago
ŌTĀKOU WHAKAIHU WAKA

MICROBIOLOGY & IMMUNOLOGY
Te Tari Maromaroiti me te Arai Mate

Objectives

To be able to:

- Describe the key components of the inflammatory response
- Describe the 5 stages of phagocytosis
- Explain the main features of the complement system

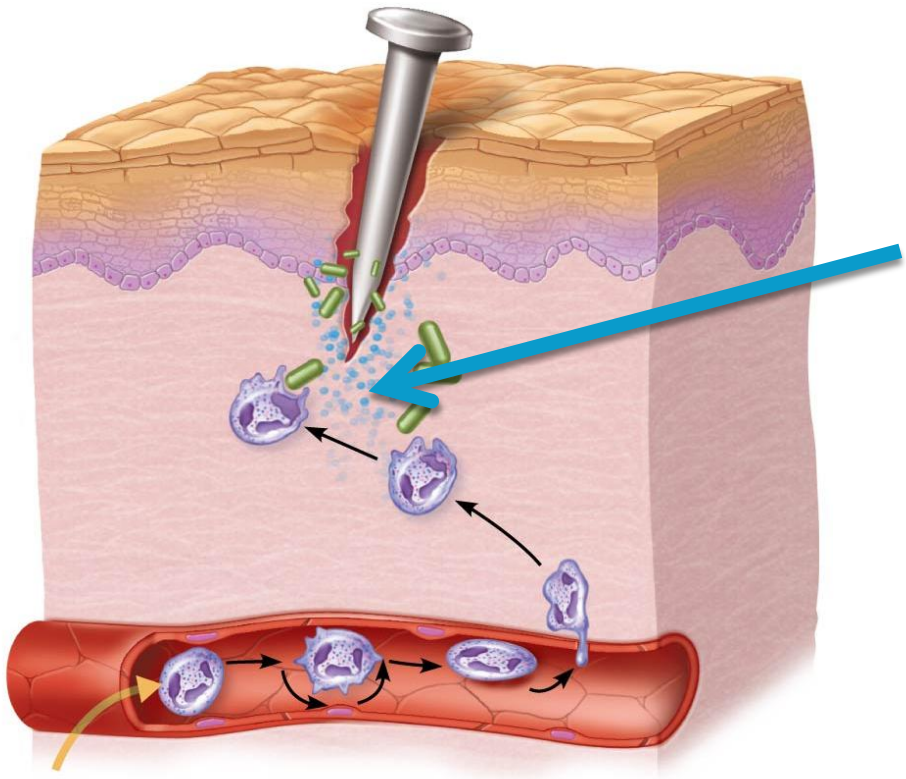
Readings:

- Marieb 10e Chapter 21 second part of Section 21.2, page 794 (Section Phagocytosis and Figure 21.2)
- Marieb 10e Chapter 21 page 795-797 (Section Inflammation: Tissue Response to Injury and Figure 21.3 and 21.4)
- Marieb 10e Chapter 21 page 798-799 (Section Complement and Figure 21.6)

3 layers of immune defense

1. Physical & Chemical Barriers (skin, mucosal membranes)
2. The Innate Immune System
3. The Adaptive Immune System

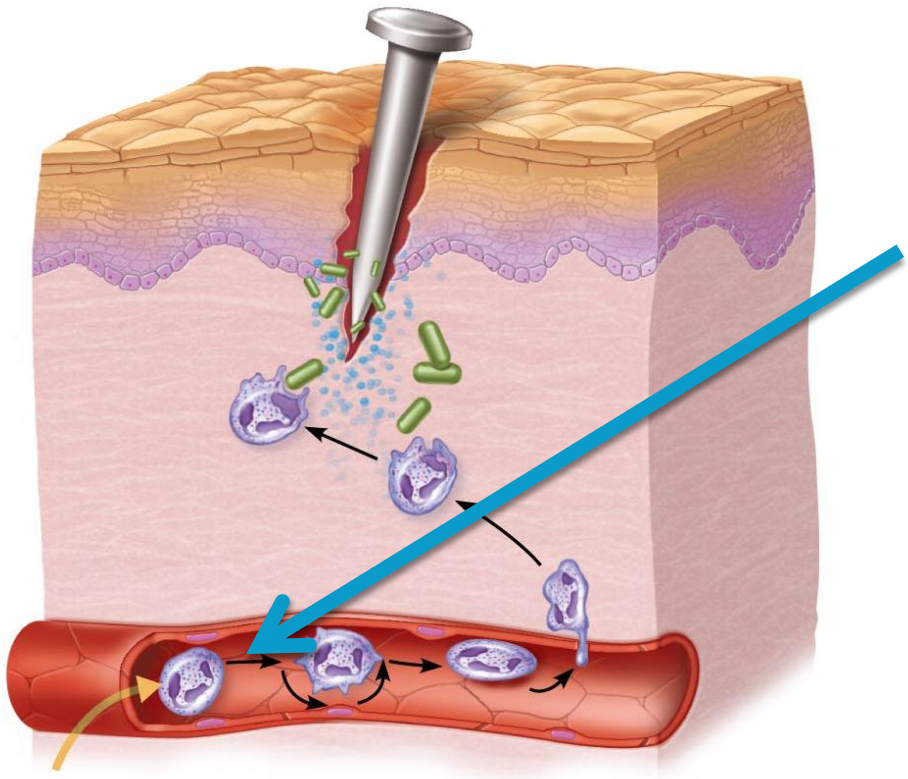
The inflammatory response



Chemical signals from tissue-resident cells act to attract more cells to the site of injury or infection

Marieb Figure 21.4

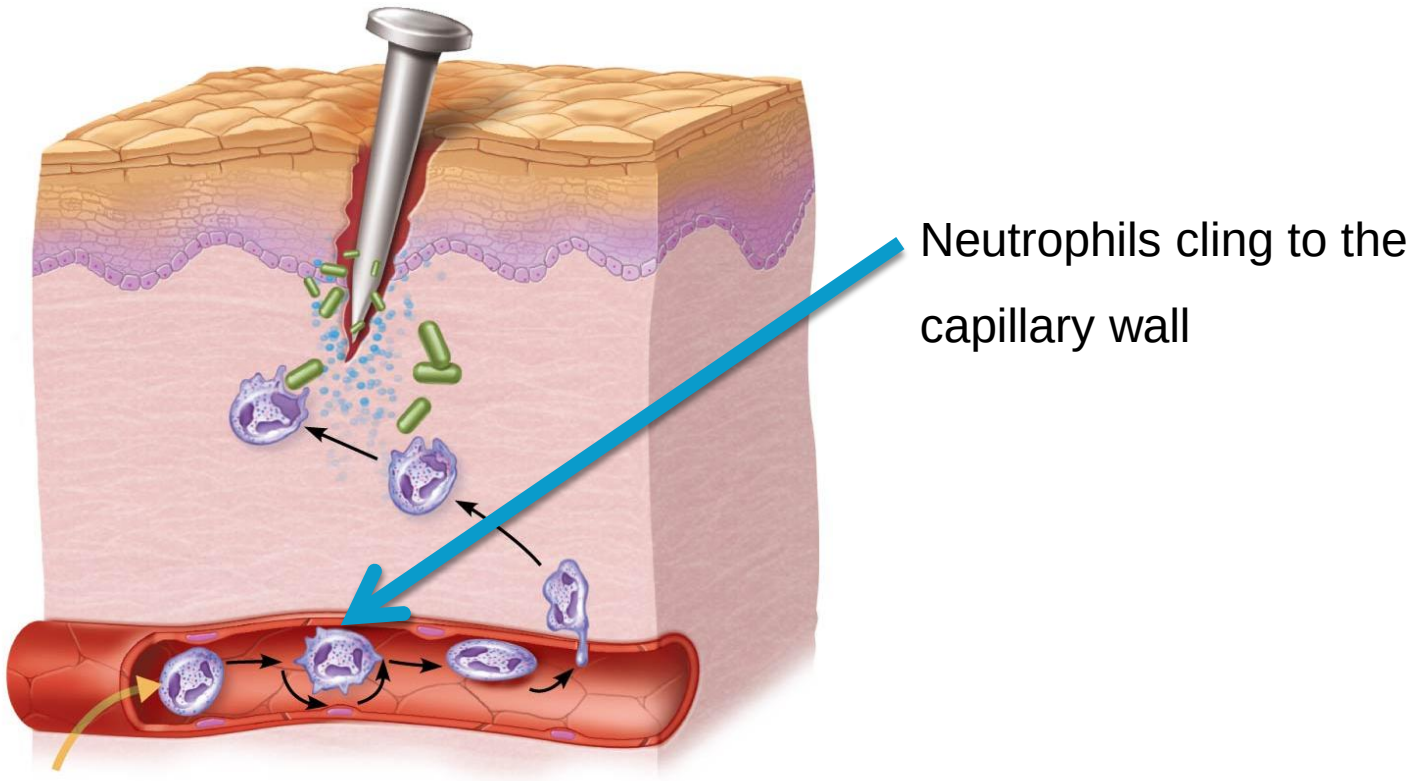
The inflammatory response



Neutrophils enter blood from the bone marrow

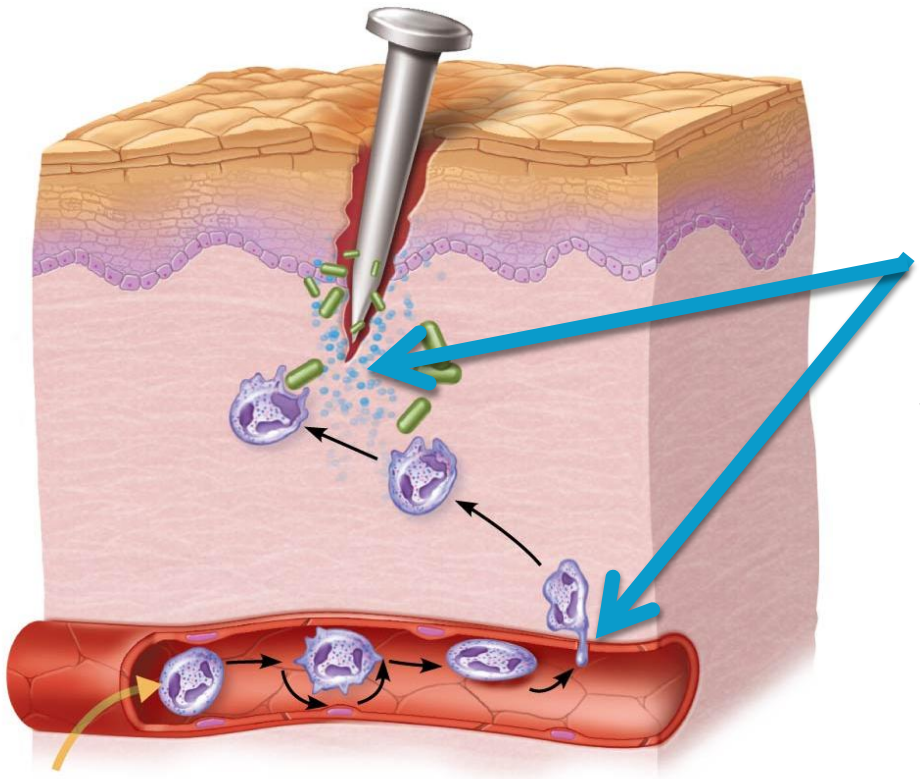
Marieb Figure 21.4

The inflammatory response



Marieb Figure 21.4

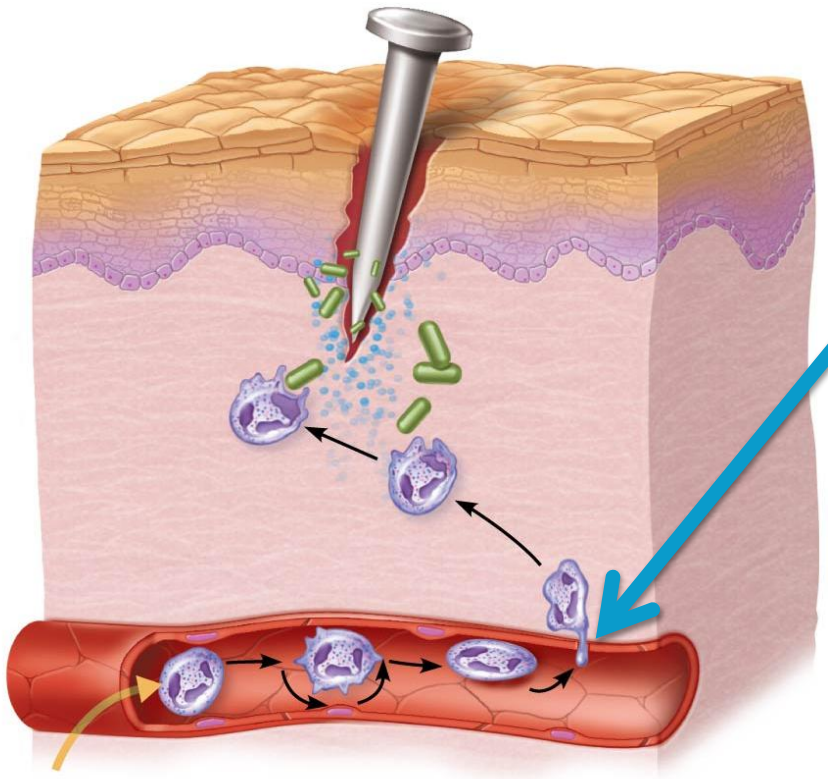
The inflammatory response



Chemical signals from tissue-resident cells dilate blood vessels and make capillaries ‘leakier’

Marieb Figure 21.4

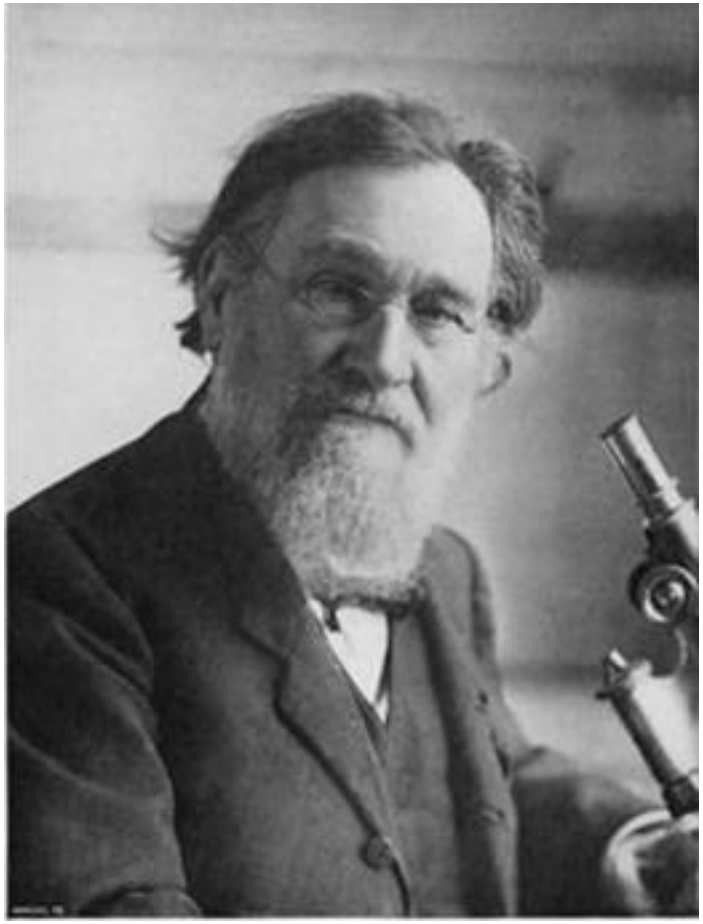
The inflammatory response



Neutrophils squeeze through the ‘leaky’ capillary wall and follow the chemical trail to the injury site

Marieb Figure 21.4

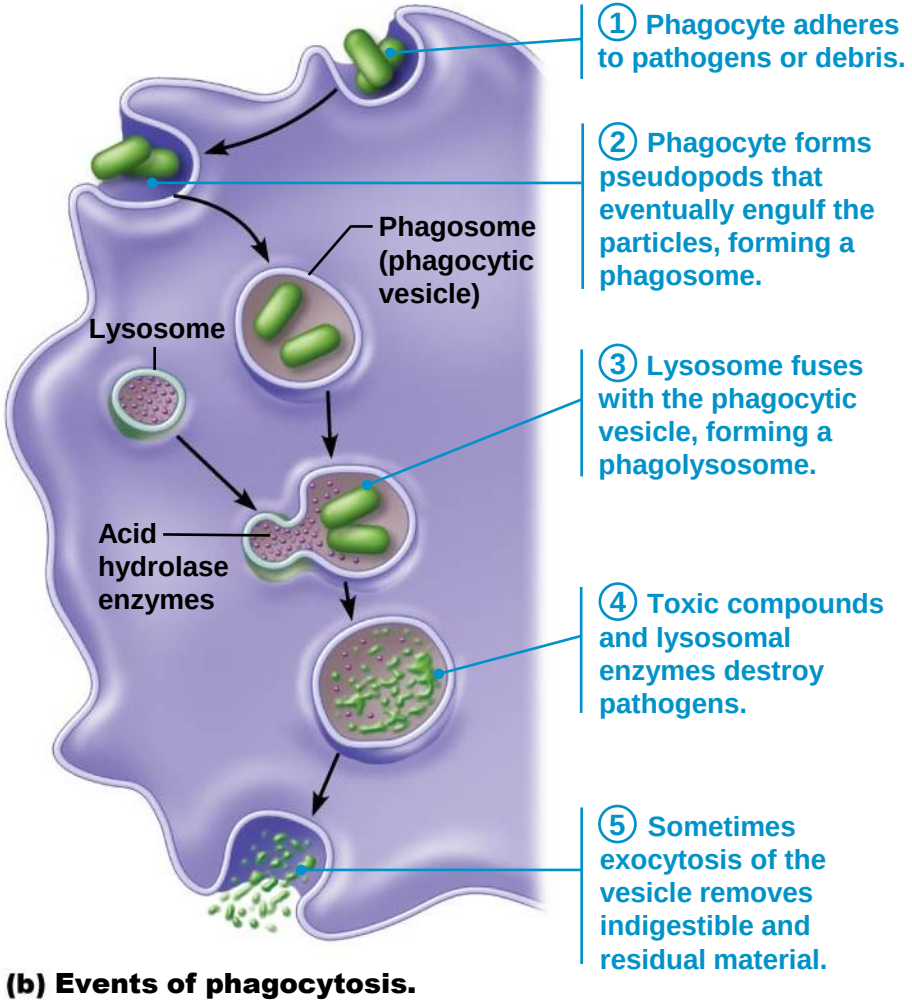
Many ***myeloid*** cells are phagocytic



In 1886-87 Elie Metchnikoff discovered the cells in the blood could ingest and destroy microbes – a process called phagocytosis

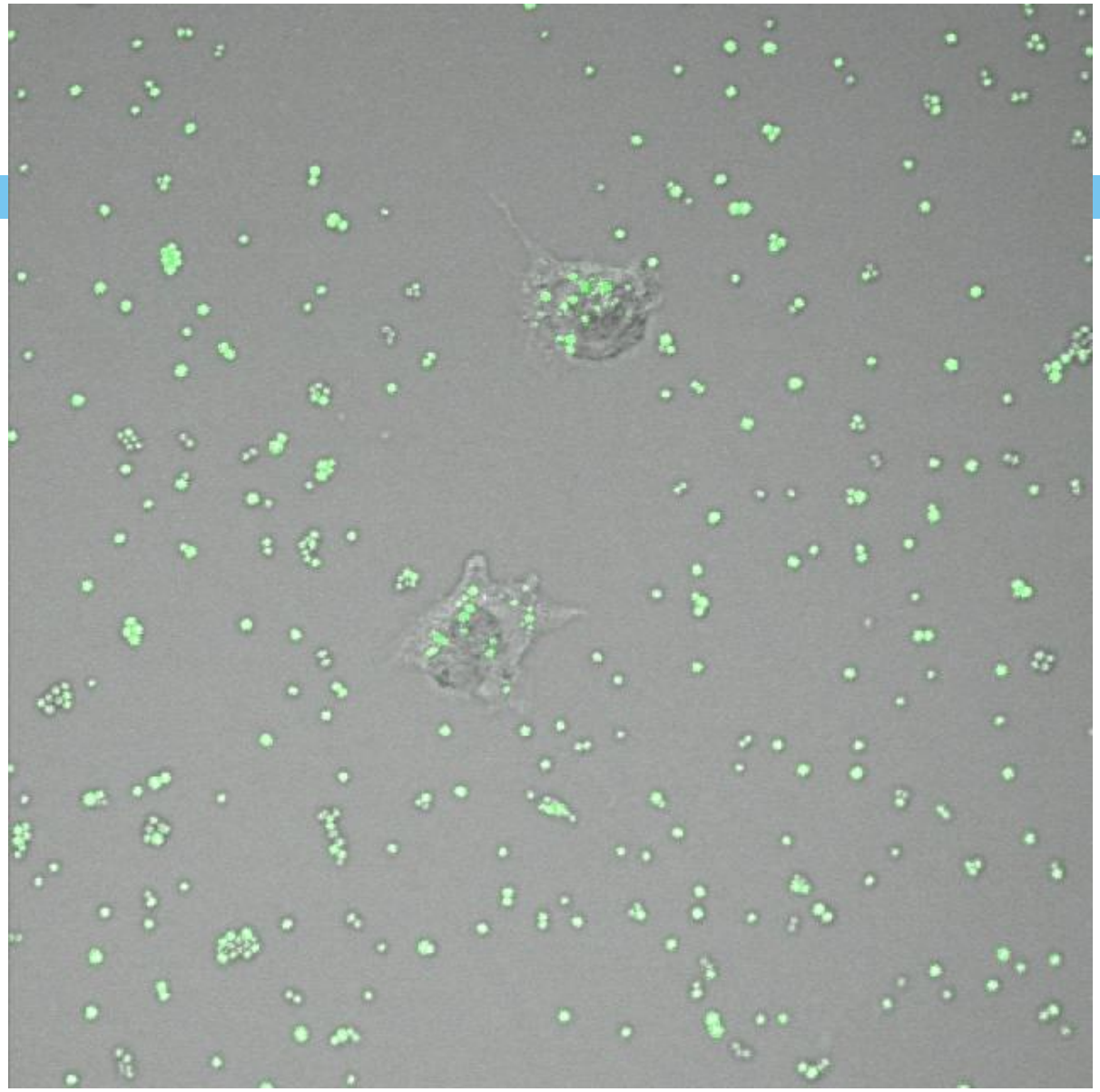
Phagein = Ancient Greek "to devour"

Stages of phagocytosis



(b) Events of phagocytosis.

Marieb Figure 21.2



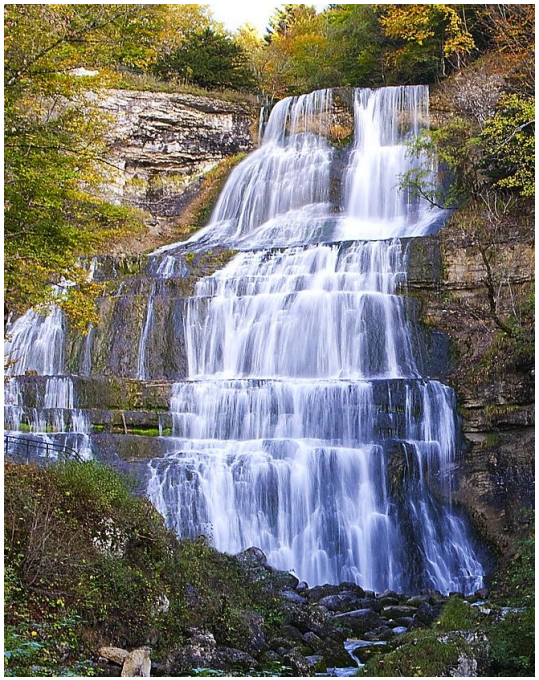
Neutrophils phagocytosing *Staphylococcus aureus* (green)
Dr Richard Sequeira, University of Auckland

Killing and digestion of phagocytosed microbes

- Low pH - acid environment
- Reactive oxygen (hydrogen peroxide) and reactive nitrogen intermediates (nitric oxide)
- Enzymes
  - Proteases
  - Lipases
  - Nucleases

The Complement Cascade

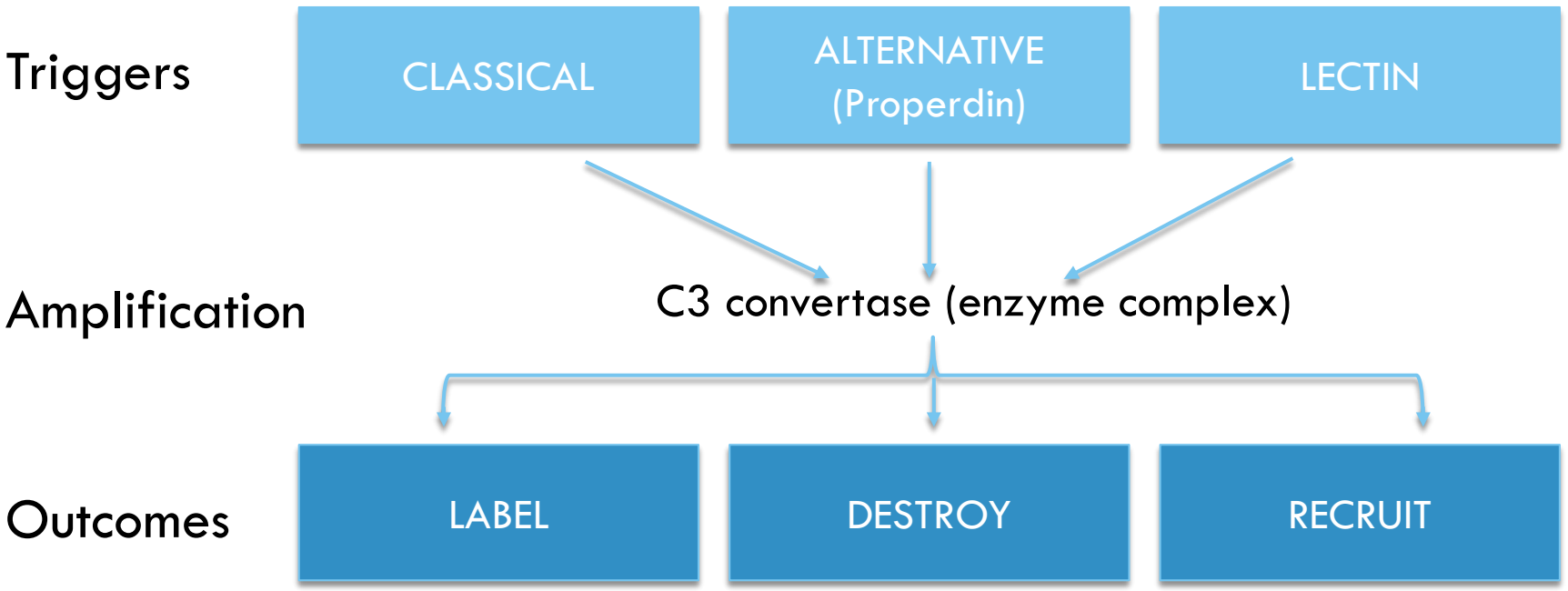
- Complement – 9 major proteins/protein complexes (C1-9) act in sequence to clear pathogens from blood and tissues
  - Label pathogens (opsonisation)
  - Recruit phagocytes (chemotaxis)
  - Destroy pathogens (lysis)



3 Complement Pathways

CLASSICAL	ALTERNATIVE	LECTIN
Antibody bound to pathogen binds complement	**Pathogen binds complement to surface/pathogen component**	**Carbohydrate components of microbes bind complement**

Complement pathways converge

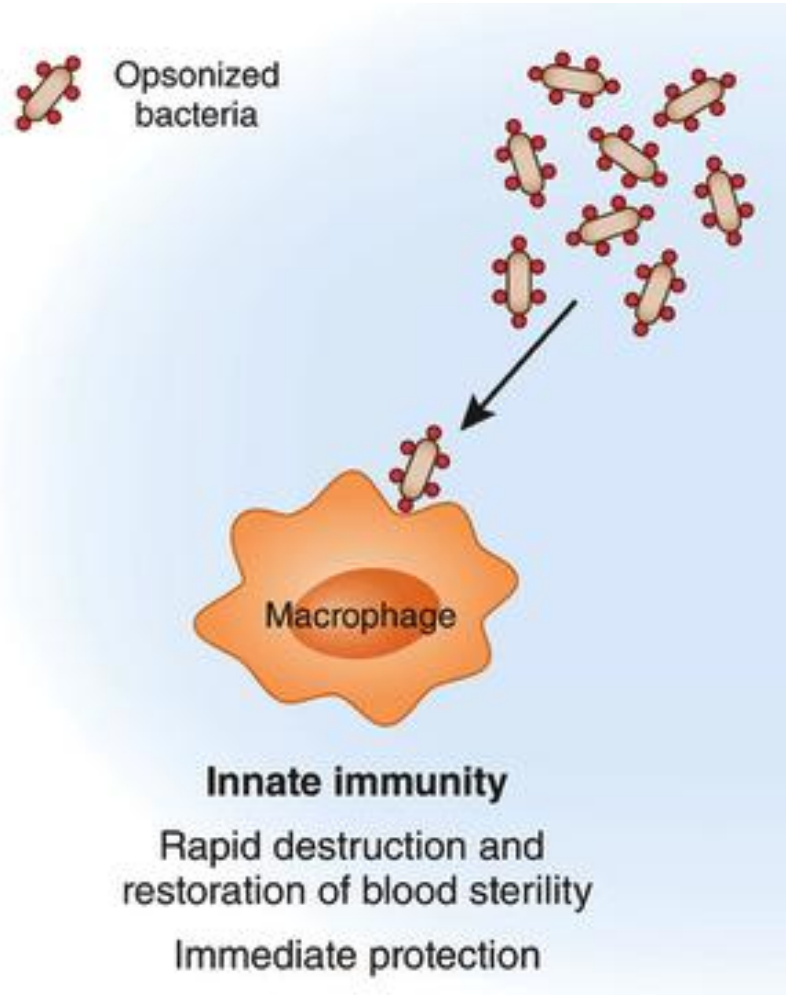


3 outcomes from the complement cascade

LABEL	DESTROY	RECRUIT
Opsonisation (labels pathogens which bind to complement receptors on phagocytes)	**Membrane Attack Complex formation: pores in bacterial cells → death**	**Complement proteins act as peptide mediators of inflammation and recruit phagocytes**
C3b	**C9**	**C3a and C5a**

Label (Opsonisation)

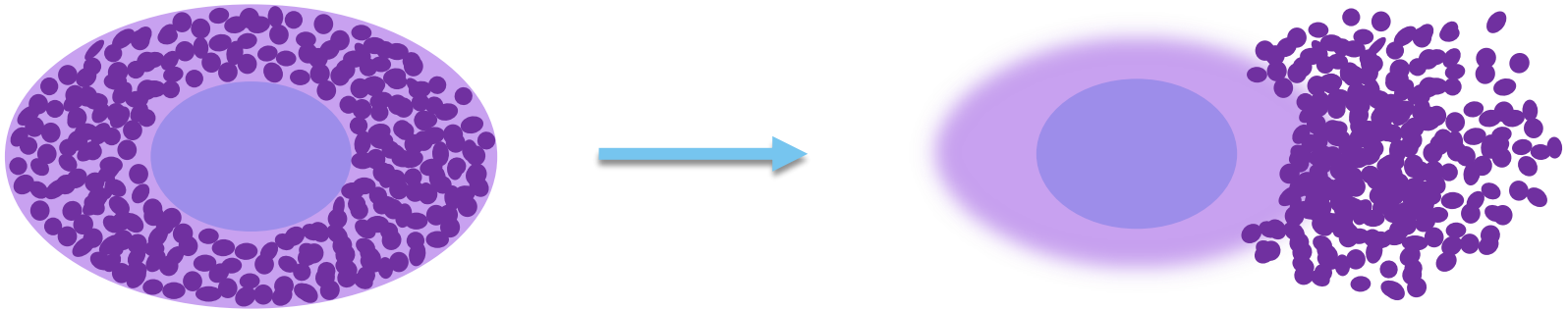
- Opsonisation = coating of a microbe with:
  - Antibody and/or
  - Complement fragment C3b



Nature Immunology 12, 1137 (2011)

Recruit

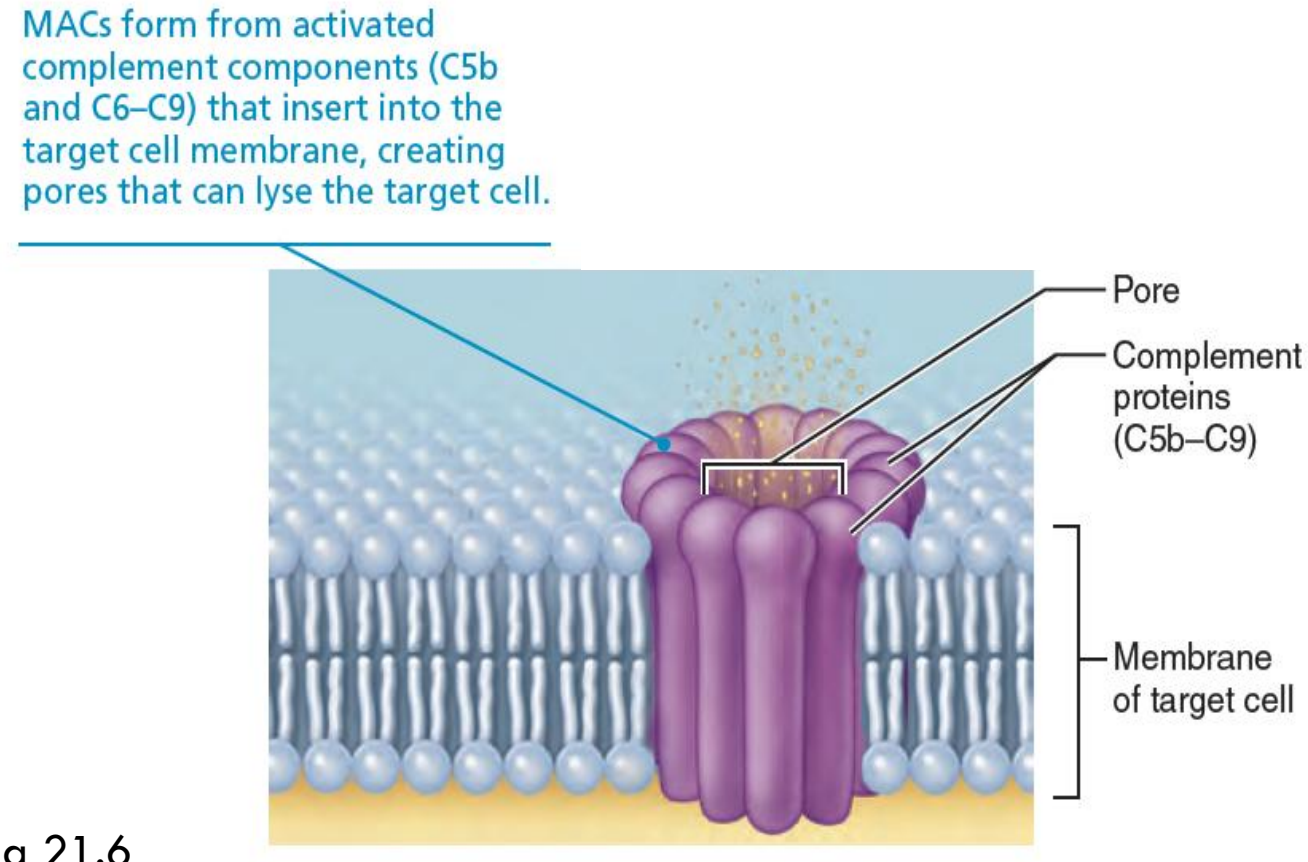
- Phagocytes attracted into site
- Mast cells degranulated by C3a and C5a



- Inflammatory mediators released including proteins that attract phagocytes

Destroy

- microbes coated with C3b are phagocytosed
- assembly of the MAC causes lysis



Marieb 10e Fig 21.6

Revision MCQ

Killing of a phagocytosed microbe requires:

a) binding and activation of toll-like receptors.
b) degranulation caused by C3a and C5.
c) anti-microbial peptides, such as defensins.
d) reactive oxygen and nitrogen intermediates.

HUBS191