

Opsonization and Phagocytosis

Antibody-mediated (type II) hypersensitivity

Cell-surface recognition → effector recruitment → cellular injury

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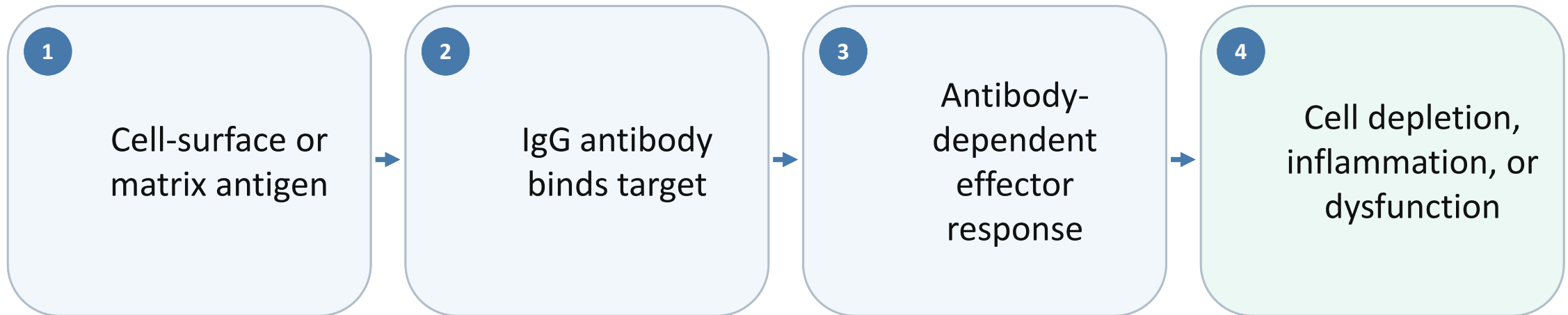
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Learning objectives

- Define opsonization and explain the role of IgG and C3b
- Trace antibody-coated target recognition through phagocytic destruction
- Differentiate phagocytosis, membrane attack, and ADCC
- Apply mechanisms to immune blood-cell destruction

Type II hypersensitivity: Antigen is target-bound

Type II responses depend on antigen location and the effector pathway



The antigen location determines the injury pattern

Cell destruction and tissue inflammation are different outcomes

Circulating cell

Antibody coats accessible cell surface

Phagocytic removal may deplete the population

Fixed tissue

Antibody deposits on matrix or basement membrane

Local inflammation may damage surrounding tissue

Which antigens may become antibody targets?

Both self and acquired determinants may initiate antibody-mediated damage

Intrinsic antigens

Normal cell or tissue structures

Autoantibodies can recognize host targets

Acquired antigens

Exogenous drug or microbial antigens on a surface

Antibody can attack a cell bearing the acquired determinant

Three mechanisms of antibody-mediated injury

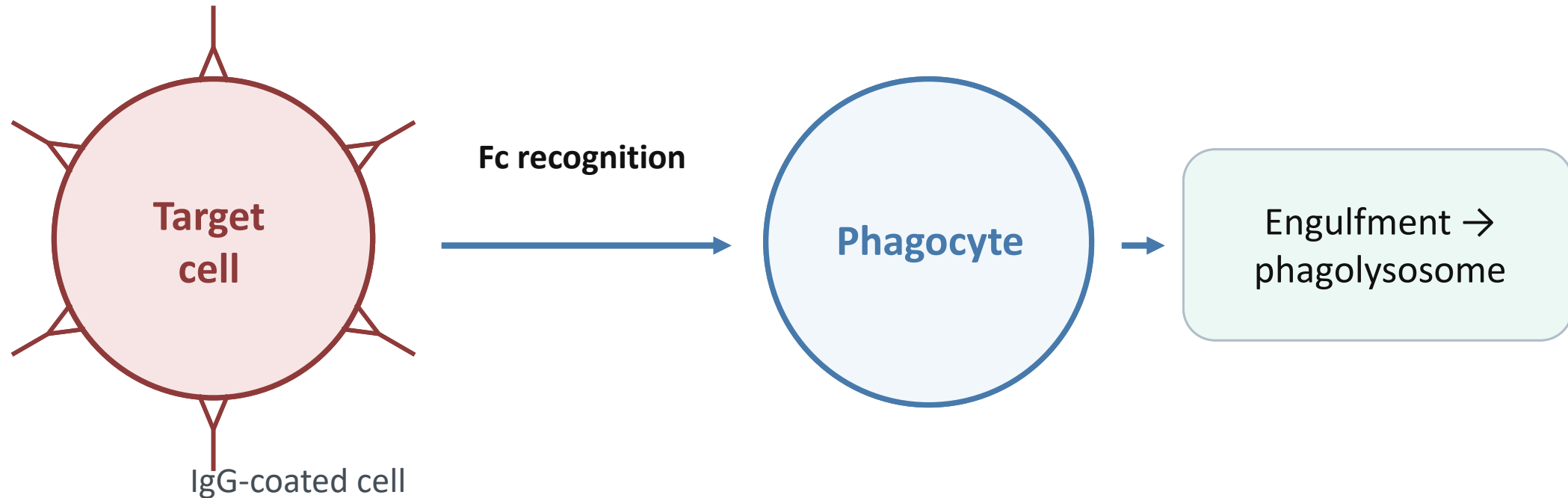
Not every antibody-coated cell is destroyed by phagocytosis alone



Sequential causal pathway

Opsonization: Coating makes a target recognizable

The opsonin creates a molecular bridge between target and phagocyte



1. Opsonin deposits on the target surface

2. Specific phagocyte receptor binds the coating

3. Receptor engagement favors ingestion

Two principal opsonins in this context

IgG and C3b provide distinct receptor-binding routes

IgG

Fab binds cell antigen; Exposed Fc is recognized

Phagocyte Fc receptors

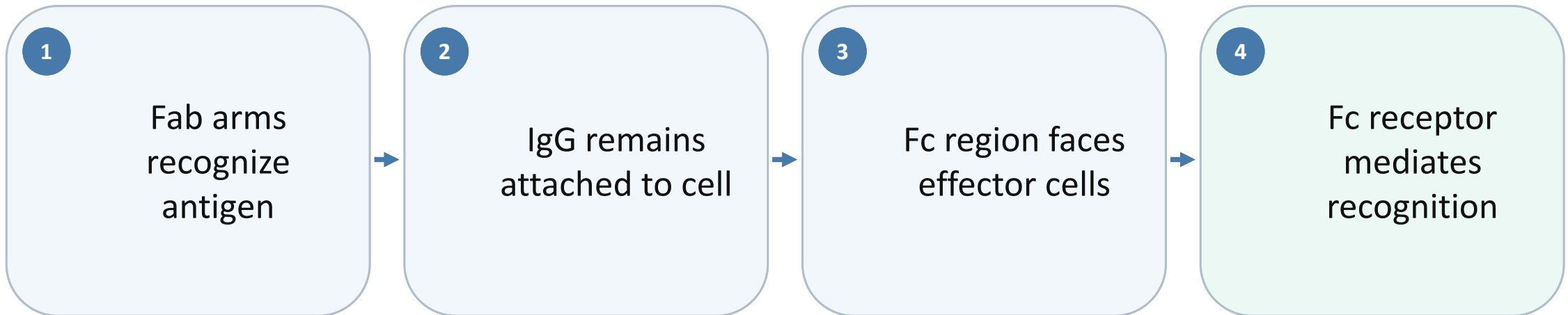
C3b

Complement cleavage product deposited on a cell

Complement receptors on phagocytes

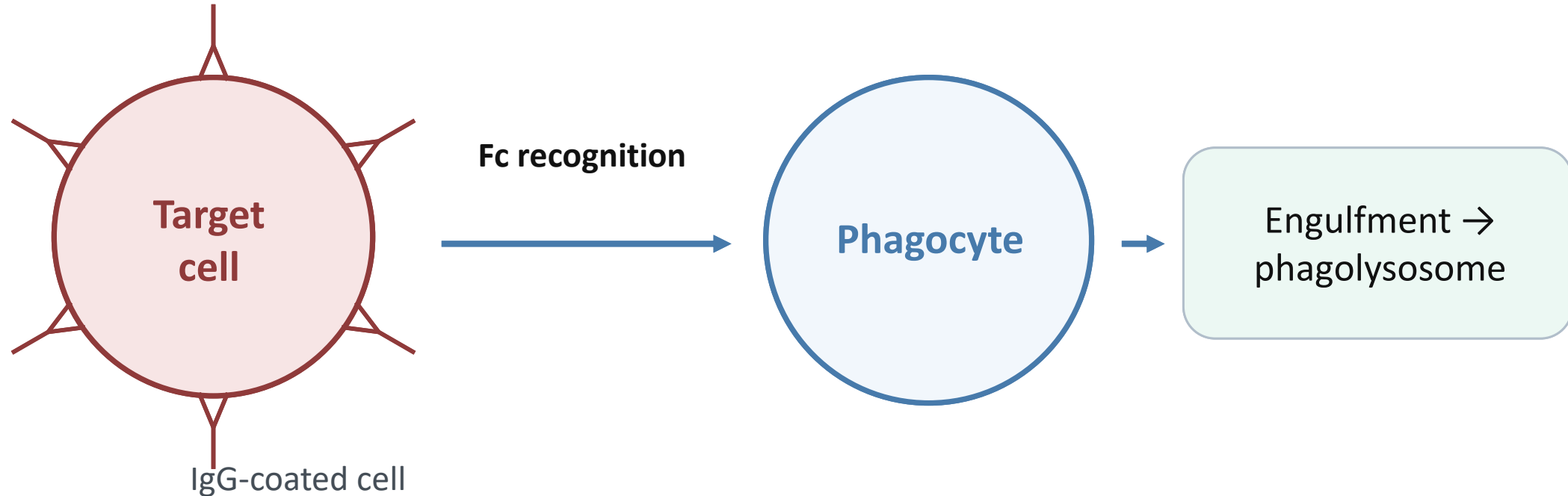
The IgG molecule performs two different tasks

Antigen specificity and effector recruitment reside in different IgG regions



Fc receptor engagement links antibody to ingestion

Fc receptors recognize Fc portions of relevant IgG subclasses



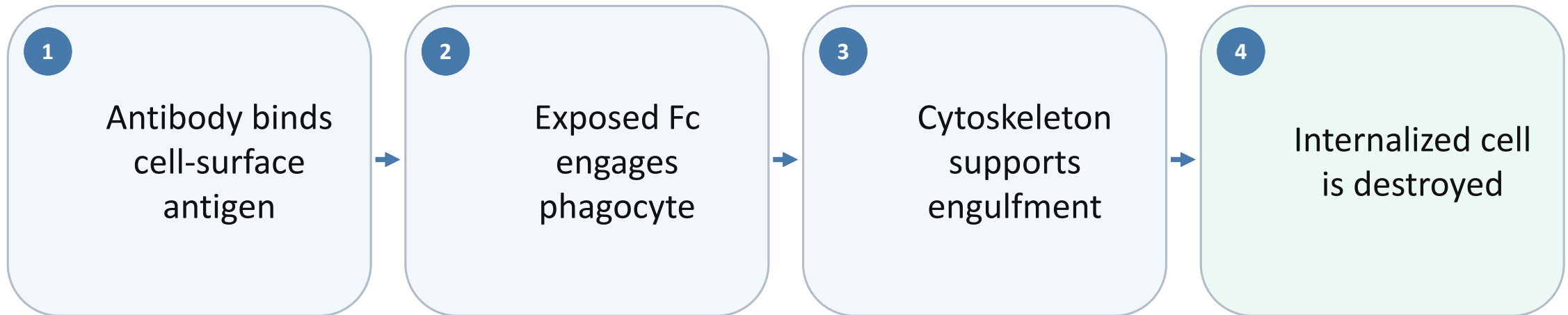
1. IgG coats an erythrocyte or other host cell

2. A macrophage or neutrophil binds the IgG Fc region

3. Target recognition precedes internalization

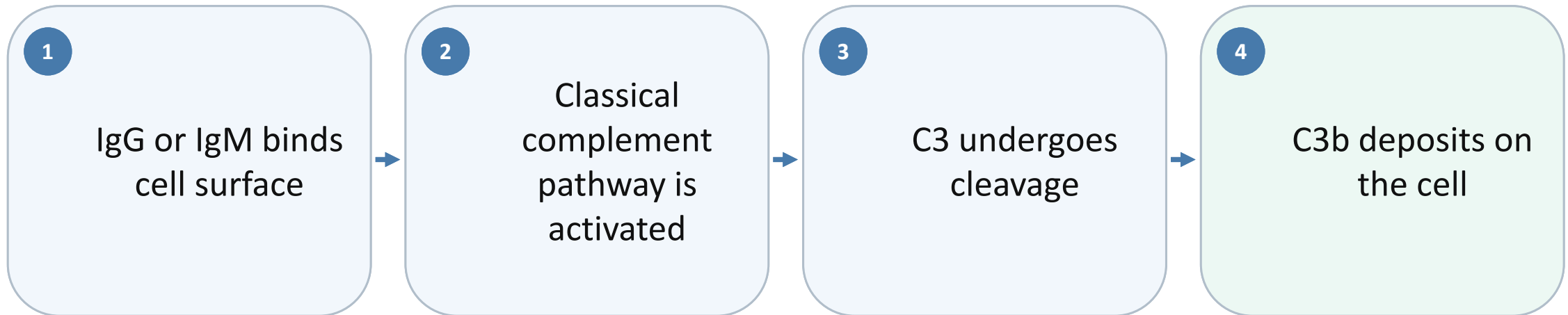
Direct IgG opsonization: Causal sequence

Binding alone is not the entire destructive process



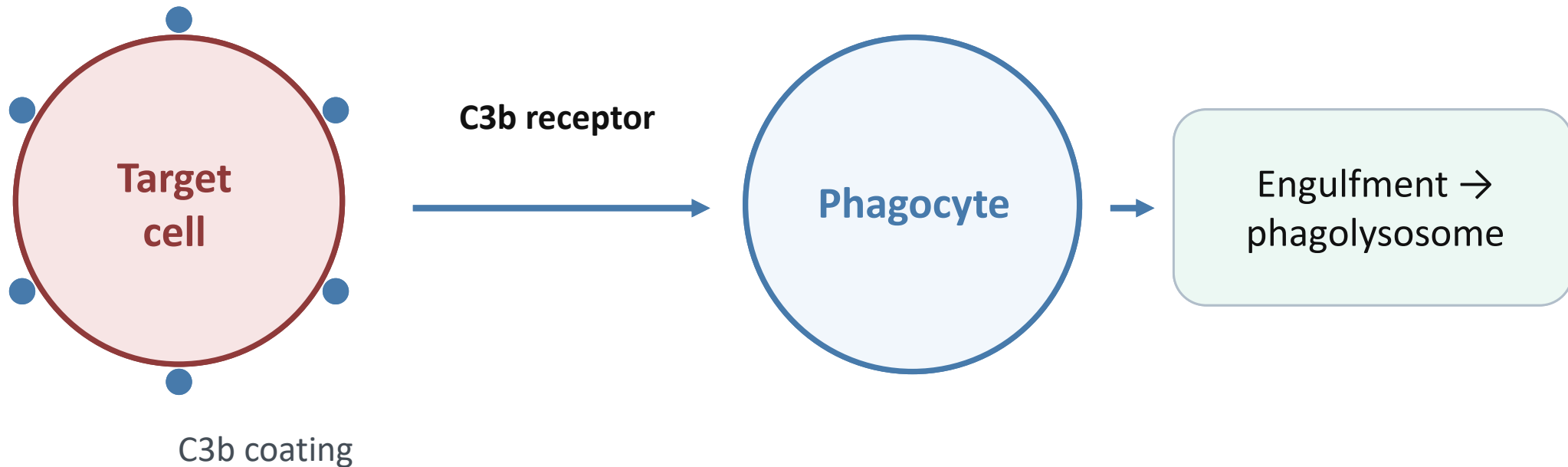
Classical complement can begin on an antibody-coated cell

IgM is important for complement activation, not direct FcγR uptake



C3b deposition changes the target surface

Complement amplifies recognition of an antibody-tagged target



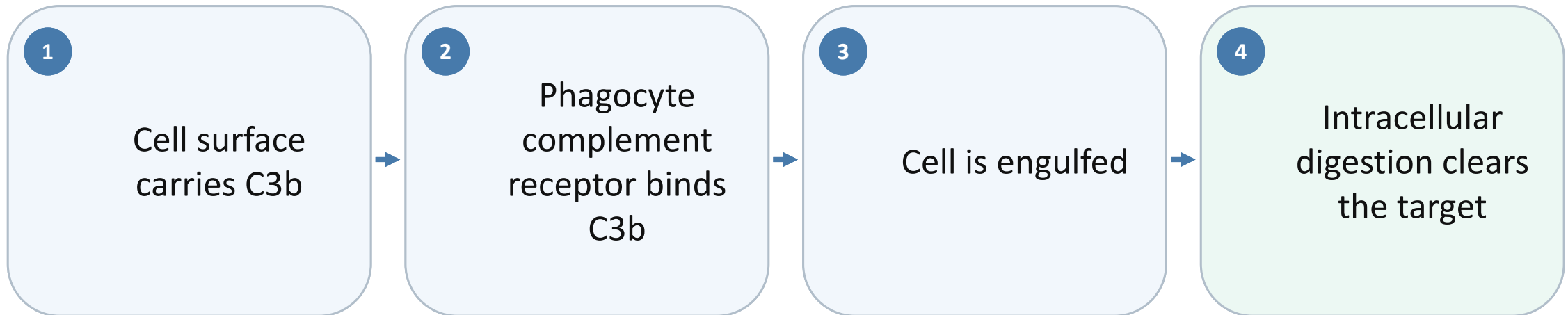
1. Complement activation yields C3 fragments

2. C3b becomes associated with the coated cell

3. Complement receptors bind deposited C3b

Complement receptors complete the bridge

C3b promotes phagocytosis by neutrophils and macrophages



IgG and IgM: Not equivalent receptor routes

Separate antibody recognition from complement-mediated opsonization

IgG-coated cell

Direct phagocyte Fc recognition is possible

Can also activate complement

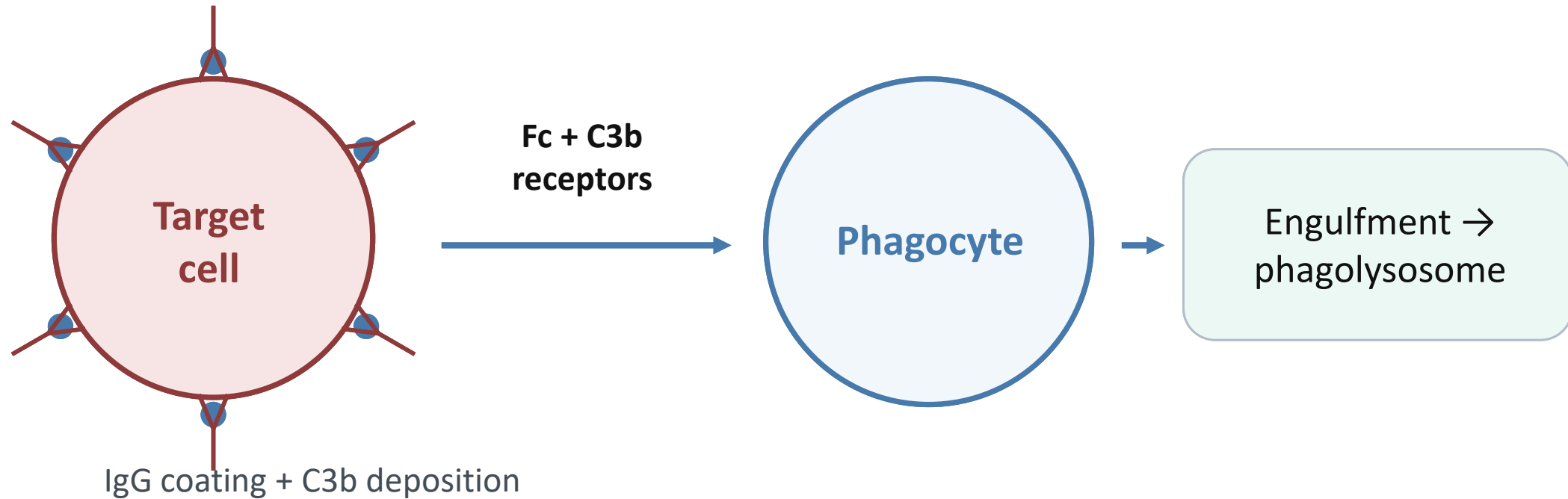
IgM-coated cell

Does not use the IgG-specific Fc receptor route

Can activate classical complement and promote C3b coating

Dual coating creates parallel recognition routes

The surface can display antibody and complement simultaneously



1. IgG exposes Fc to Fc receptors

2. Complement deposits C3b on the same target

3. Either route may support phagocyte attachment

An opsonin is not a toxin

Distinguish a recognition tag from a membrane-disrupting effector

Opsonization

Marks a particle for receptor-dependent ingestion

Requires a functional responding phagocyte

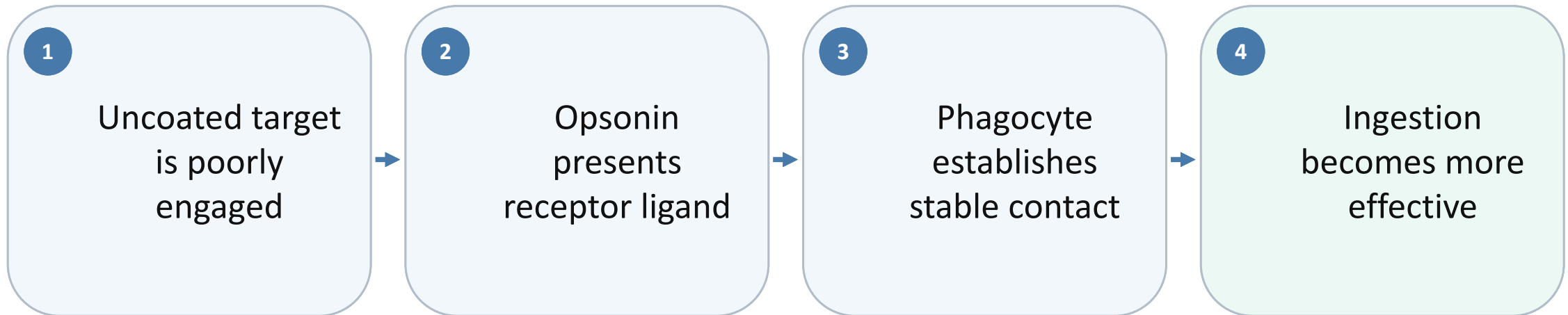
Membrane attack

Damages the target membrane directly

Causes osmotic cell lysis

Why recognition can be more efficient after coating

The receptor sees the deposited opsonin rather than the underlying antigen



Professional phagocytes in this mechanism

Both cell classes participate in antibody-dependent effector responses

Macrophage

Recognizes IgG Fc and deposited C3b

Engulfs and degrades antibody-coated cells

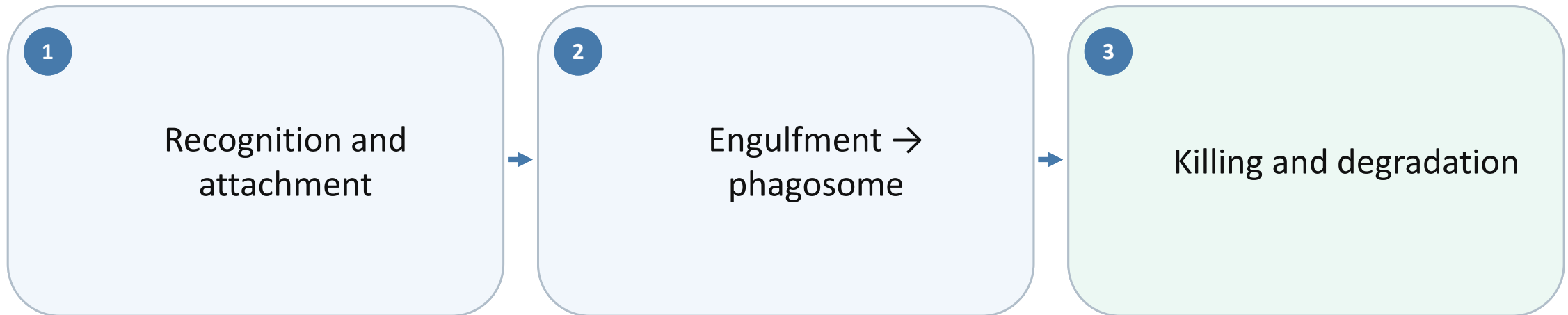
Neutrophil

Expresses opsonin-binding receptors

Can ingest targets and release injurious mediators

Phagocytosis has three major stages

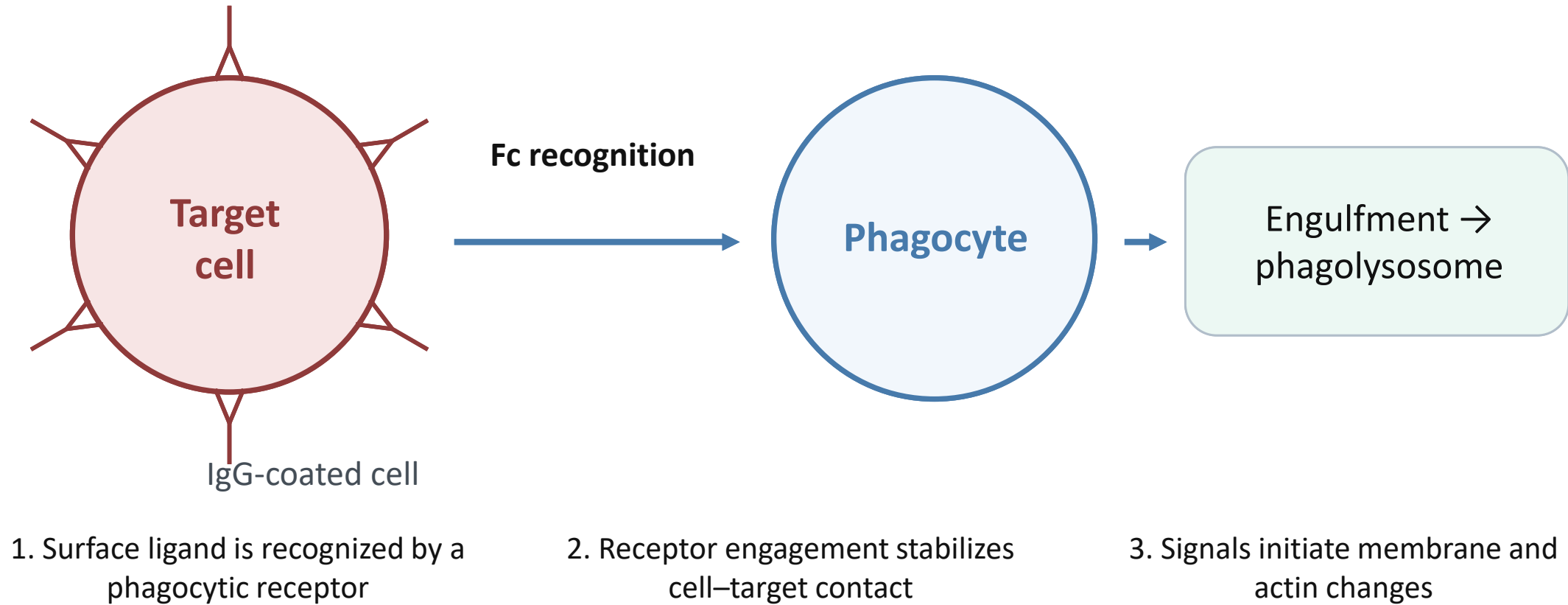
The generalized sequence also applies to ingestion of antibody-coated targets



Sequential causal pathway

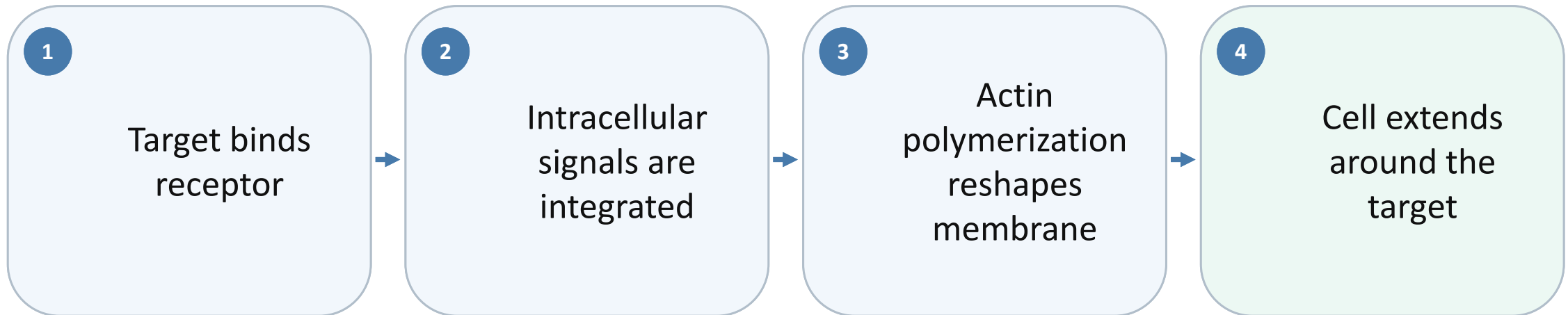
Attachment precedes membrane remodeling

Physical proximity is not equivalent to receptor-mediated uptake



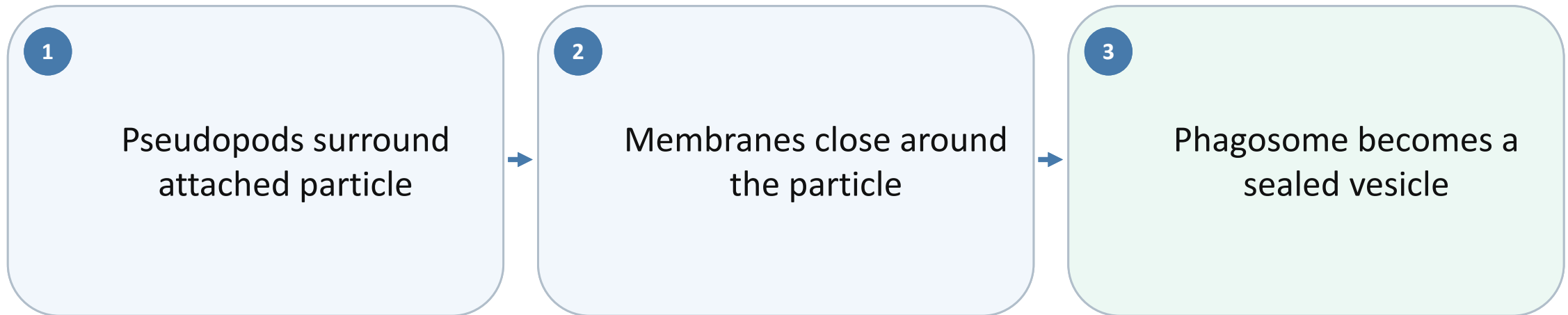
Receptor signaling reorganizes actin

Cytoskeletal remodeling drives engulfment



Engulfment creates an intracellular compartment

The ingested target is moved into a membrane-bound vacuole



Sequential causal pathway

Phagosome and lysosome are separate initially

Fusion connects uptake to degradation

Phagosome

Newly formed vesicle around ingested material

Contains the engulfed target

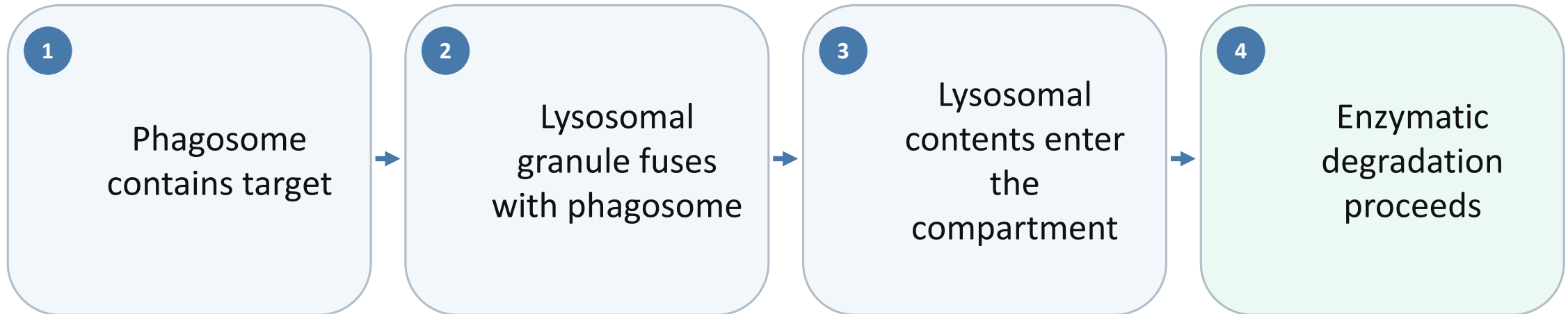
Lysosome / granule

Organelle containing hydrolytic contents

Supplies enzymes to the phagocytic compartment

Formation of the phagolysosome

The phagolysosome is the destructive compartment



Intracellular destruction employs multiple effectors

Digestion is not caused by receptor binding alone

Lysosomal enzymes

Digest proteins and other internalized material

Work within the phagolysosome

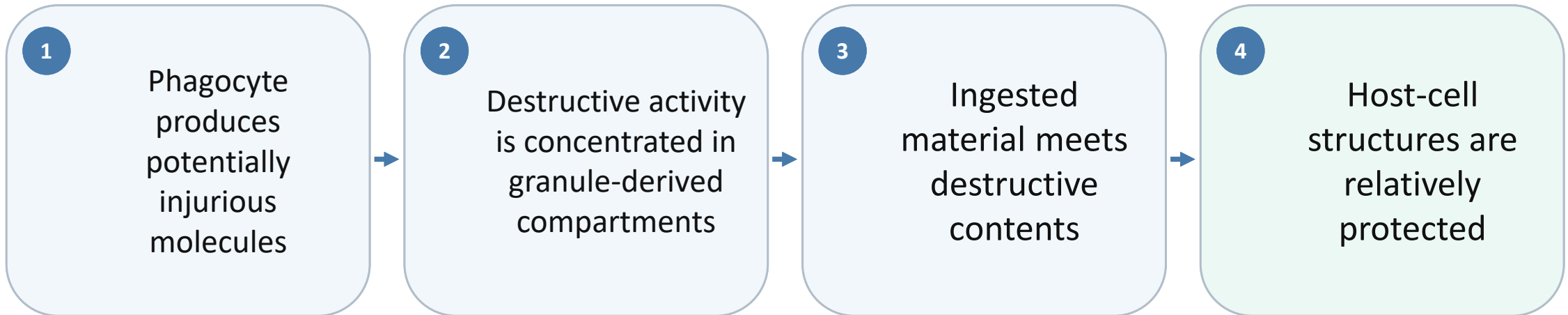
Reactive intermediates

Reactive oxygen and nitrogen species contribute

Support killing and degradation after activation

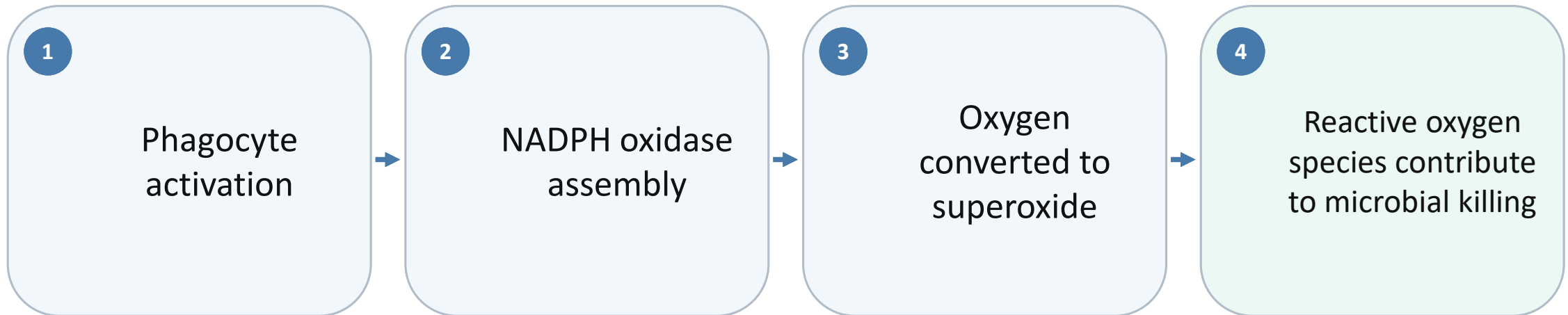
Compartmentalization protects the phagocyte

Normal phagocytosis separates potent effectors from the cytoplasm



Respiratory burst: An oxidative mechanism

The respiratory burst is a phagocyte effector function



Phagocytosis and extracellular release differ

Where effectors are released governs collateral tissue injury

Intracellular pathway

Target is ingested into a phagolysosome

Contents degrade within the cell

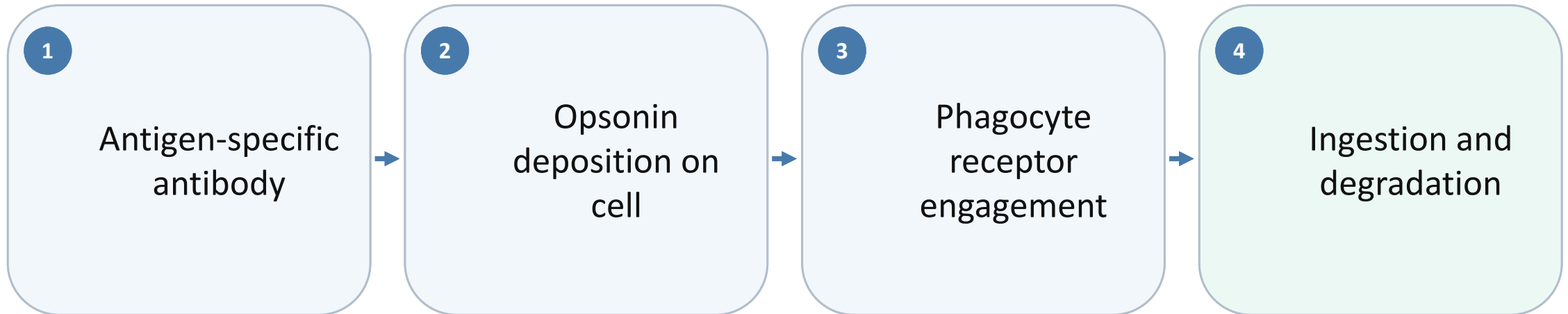
Extracellular release

Activated leukocytes release enzymes or ROS outside

Surrounding tissues may be injured

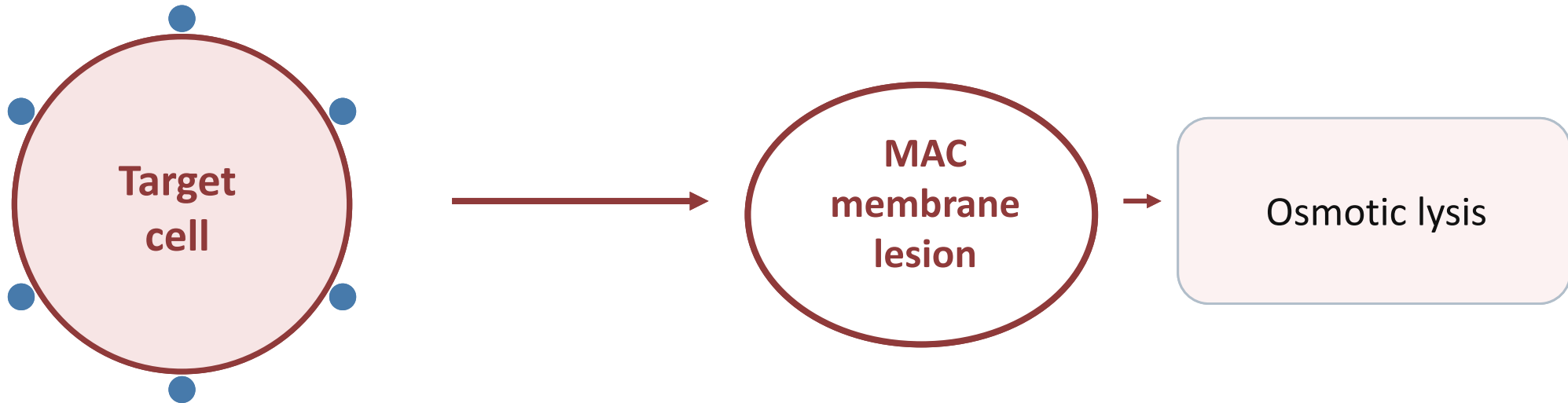
Complete cell depletion requires several linked events

An intact molecular and cellular chain produces antibody-dependent depletion



The membrane attack complex is a distinct route

This is direct complement-mediated lysis, not engulfment



1. Complement activation can proceed to terminal components

2. Membrane attack complex disrupts a lipid bilayer

3. Osmotic lysis destroys susceptible targets

C3b opsonization versus terminal complement attack

Complement is capable of both tagging and lysing cells

C3b branch

Deposits a receptor ligand on cell surface

Enhances phagocyte uptake

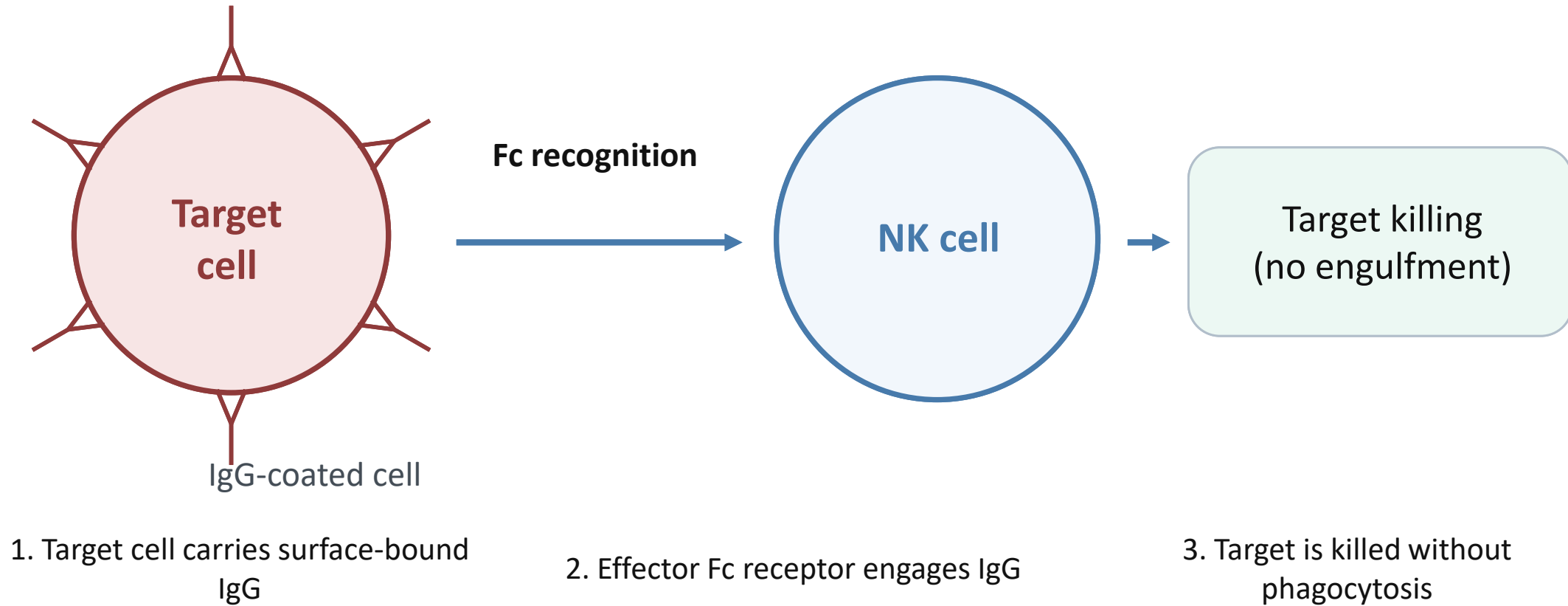
Membrane attack branch

Assembles a membrane-disrupting complex

Induces target-cell lysis

ADCC recognizes IgG but avoids engulfment

Antibody-dependent cellular cytotoxicity is a separate pathway



Which cells can execute ADCC?

Effector identity and outcome both matter

Natural killer cell

Principal effector highlighted by Robbins

Fc-dependent recognition leads to target killing

Macrophage

Can also mediate antibody-dependent killing

Fc receptor involvement does not guarantee phagocytosis

ADCC is not synonymous with phagocytosis

The presence or absence of engulfment is decisive

Phagocytosis

Target is internalized

Destruction inside a phagolysosome

ADCC

Effector binds an antibody-coated target

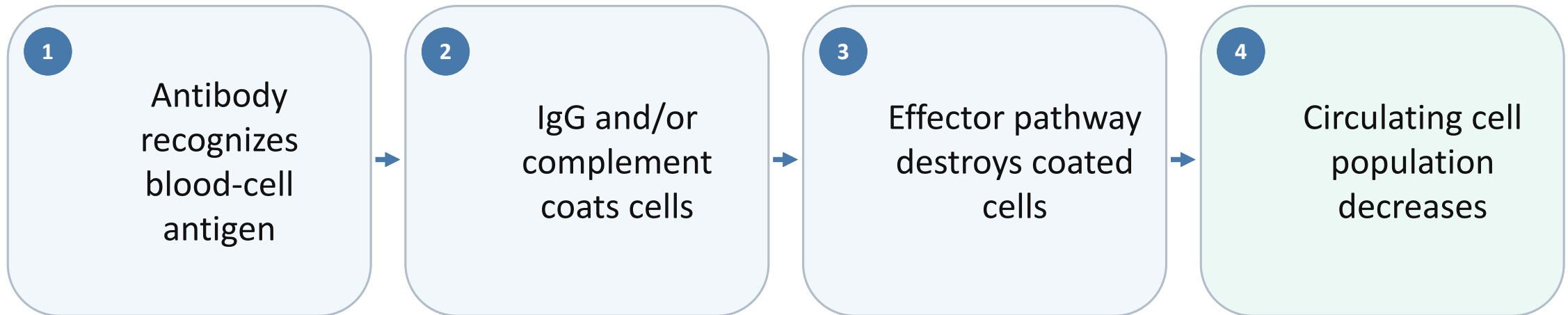
Killing occurs without ingestion

What is known about ADCC in disease?

- ADCC as a possible antibody-dependent destructive mechanism
- NK cells and macrophages can bind the Fc fragment of cell-bound IgG
- Its contribution to common hypersensitivity disorders is uncertain
- Do not attribute a specific clinical cytopenia predominantly to ADCC without evidence

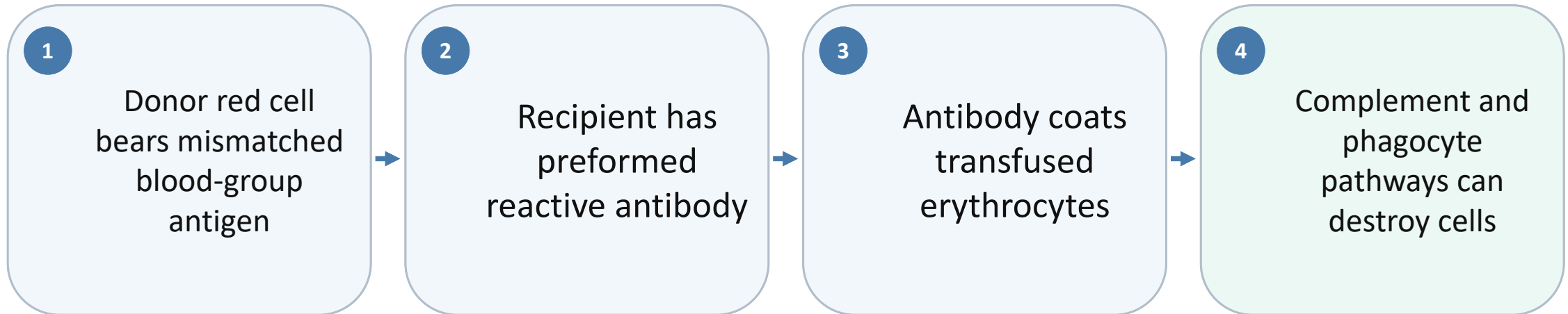
Clinical theme: Loss of circulating blood cells

Different blood-cell targets lead to different clinical syndromes



Incompatible transfusion: Antigenic mismatch

Pre-existing antibody makes target recognition possible



Transfusion reaction: The target is the donor cell

The donor–recipient antigen difference initiates the reaction

Target

Transfused red blood cell

Bears antigen against which recipient antibody reacts

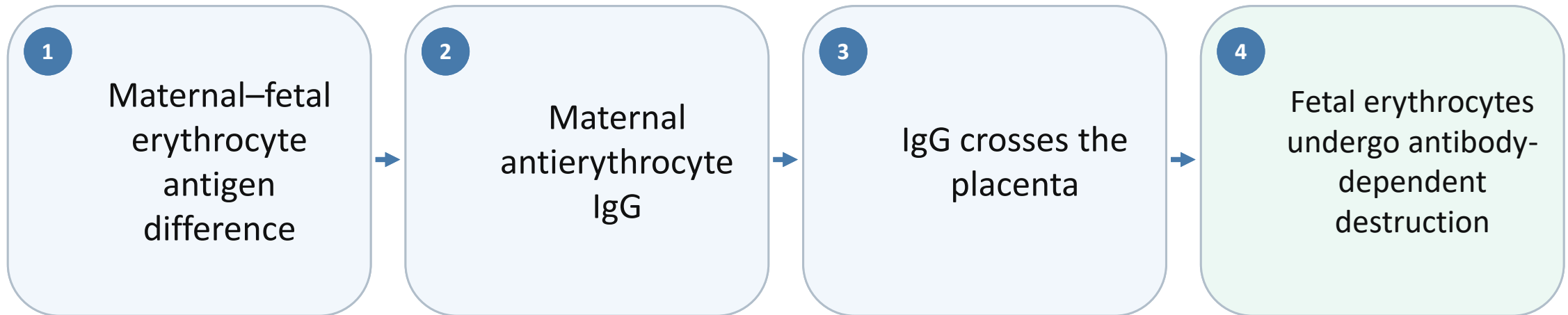
Effector context

Recipient antibody and complement

Can promote antibody-dependent cell destruction

Fetal and neonatal hemolysis: Maternal antibody

Transplacental IgG establishes the link between maternal immunity and fetal injury



Why the IgG class matters in fetal injury

Do not equate every maternal antibody response with fetal hemolysis

Maternal IgG

Can cross the placenta

May bind fetal red-cell antigens

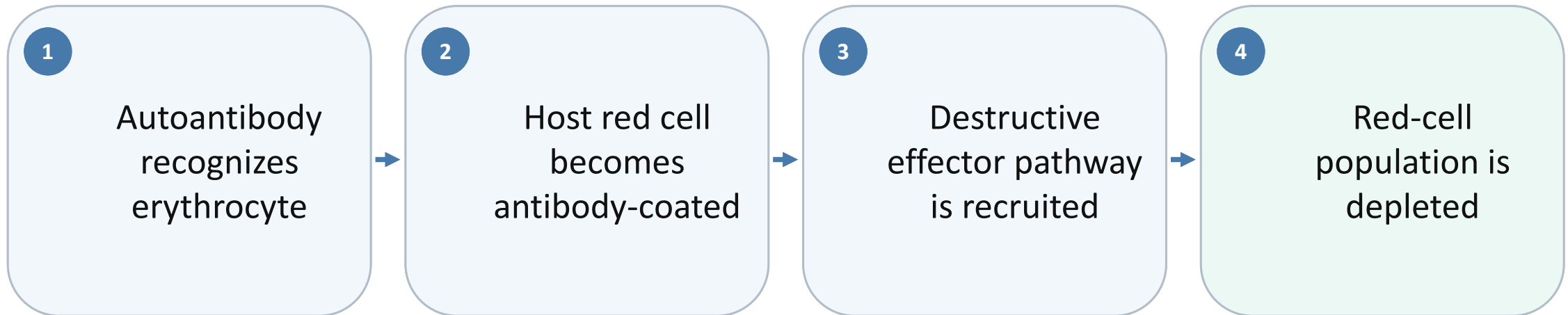
Complement-associated effects

Can occur after antibody deposition

The central source claim is IgG-mediated fetal-cell destruction

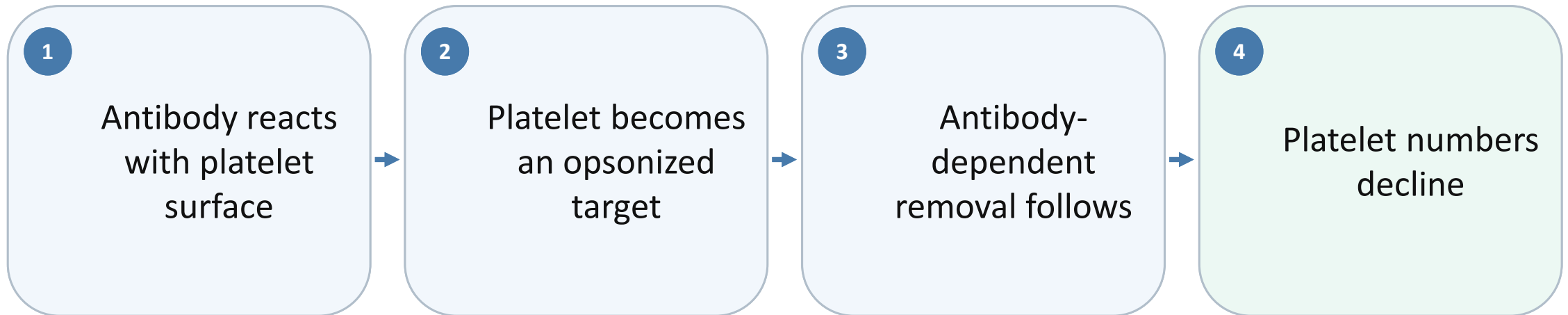
Autoimmune hemolytic anemia: A self-cell target

An autoantibody can make a normal host cell a target



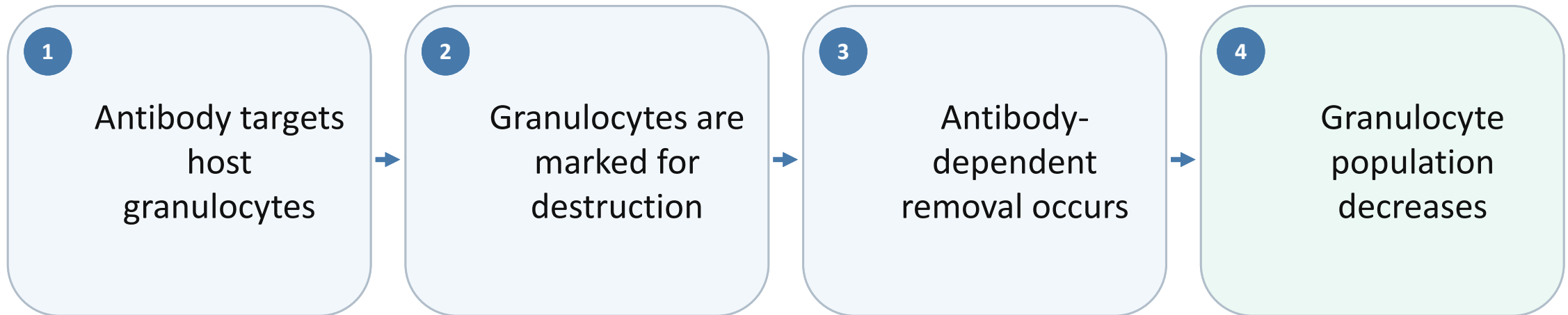
Autoimmune thrombocytopenia: Target shifts to platelets

Mechanism is shared with other immune cytopenias; The target differs



Immune agranulocytosis: Granulocyte depletion

Blood-cell specificity determines which lineage is depleted



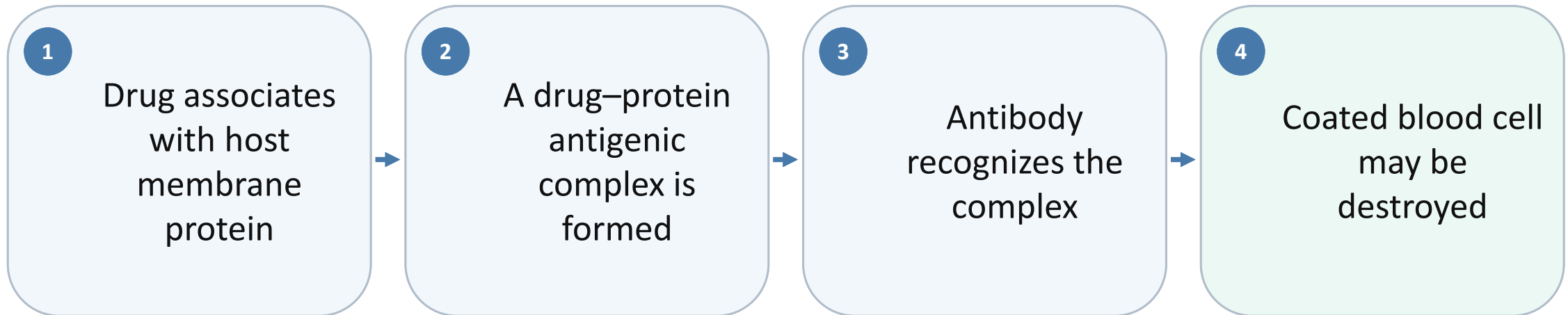
Three autoimmune cytopenias: One mechanism

The clinical label follows the affected cell lineage

Target cell	Named disorder	Core antibody-mediated event
Erythrocyte	Autoimmune hemolytic anemia	Antibody-dependent RBC destruction
Platelet	Autoimmune thrombocytopenia	Antibody-dependent platelet destruction
Granulocyte	Immune agranulocytosis	Antibody-dependent granulocyte destruction

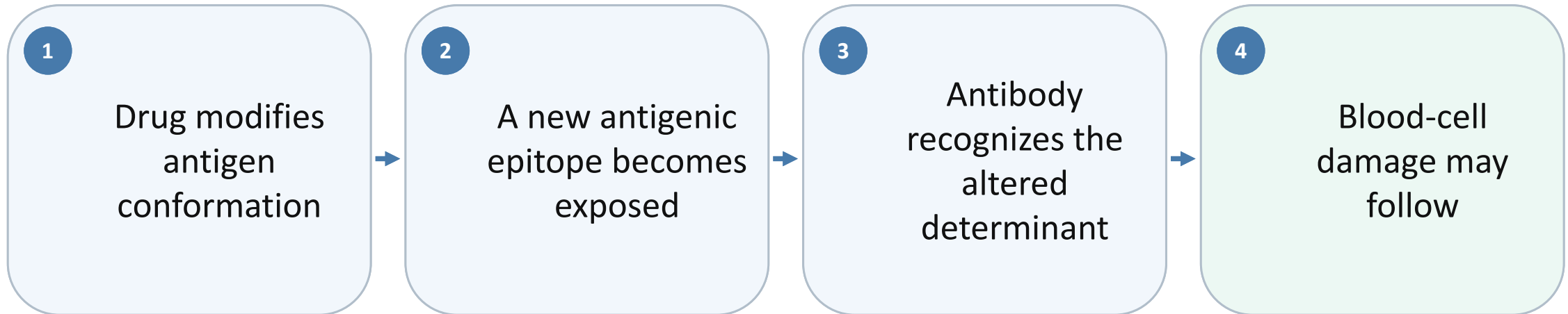
Drug-associated injury: Drug–protein complex

The drug creates an acquired antigenic target on a host cell



Drug-associated injury: Altered epitope

Antigen modification can change recognition without changing cell lineage



Two drug mechanisms are not identical

Both mechanisms produce antibody reactivity toward a host-cell surface

Drug–protein complex

Drug binds a cell-membrane protein

Antibody recognizes the composite antigen

Drug-altered antigen

Drug changes antigen conformation

Antibody recognizes a newly generated
epitope

Circulating cells versus basement membranes

Antigen anchoring changes what an effector cell can do

Circulating blood cell

Can be physically engulfed after opsonization

Depletion dominates the explanatory pathway

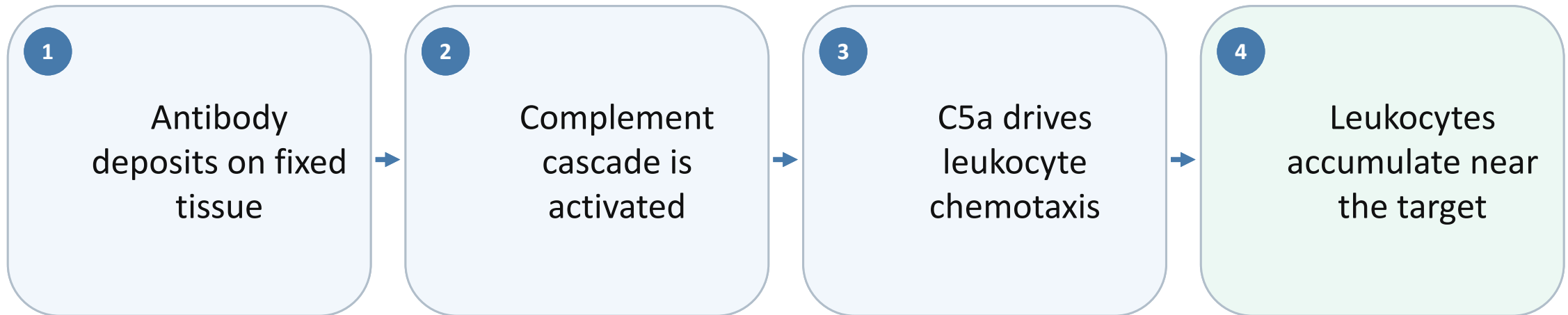
Fixed matrix

Cannot be removed like an intact circulating cell

Inflammatory mediator release dominates injury

Complement can recruit inflammatory leukocytes

Complement mediates both opsonization and inflammatory recruitment



Anaphylatoxins amplify vascular reactions

The same complement response can change leukocyte traffic and vascular leakage

C3a

Generated during complement activation

Contributes to increased vascular permeability

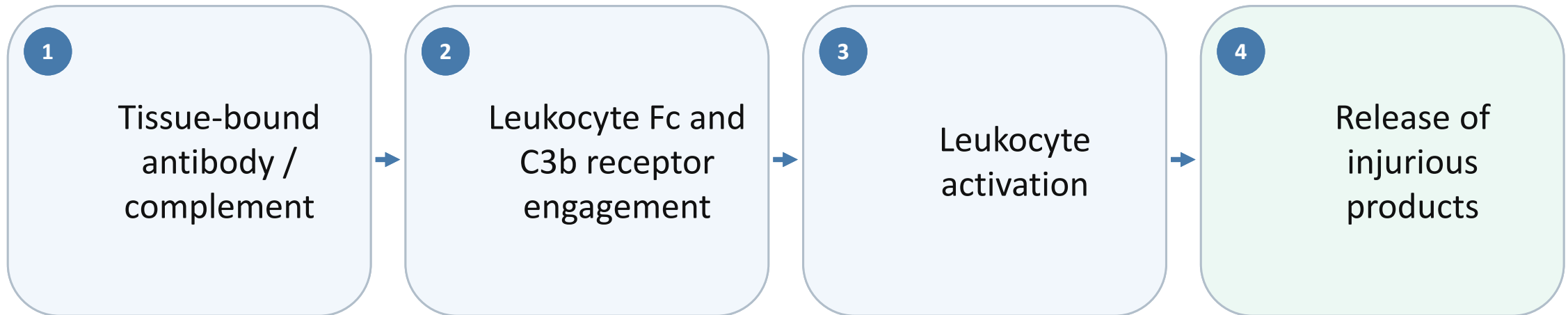
C5a

Chemotactic and anaphylatoxic activity

Promotes recruitment and permeability

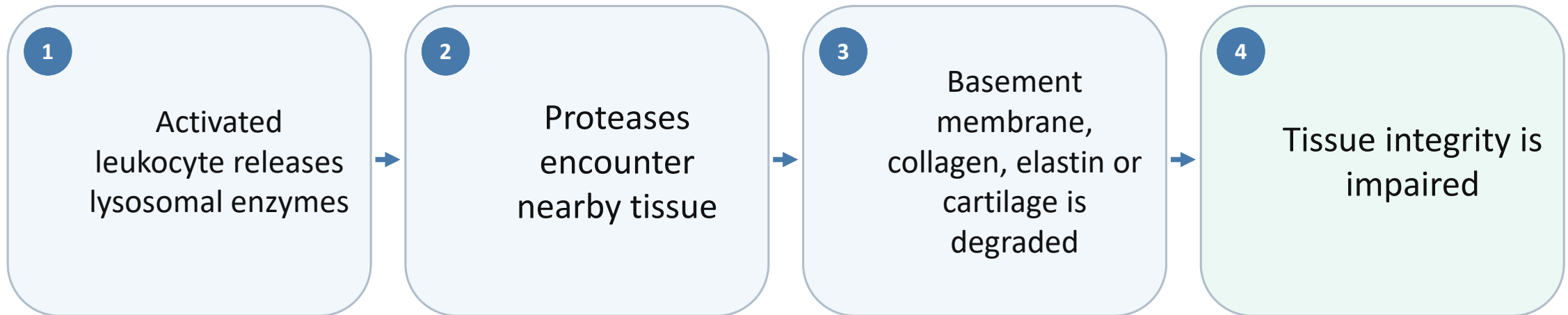
Fc and complement receptors can activate leukocytes

Surface recognition can trigger inflammation without engulfing the fixed tissue



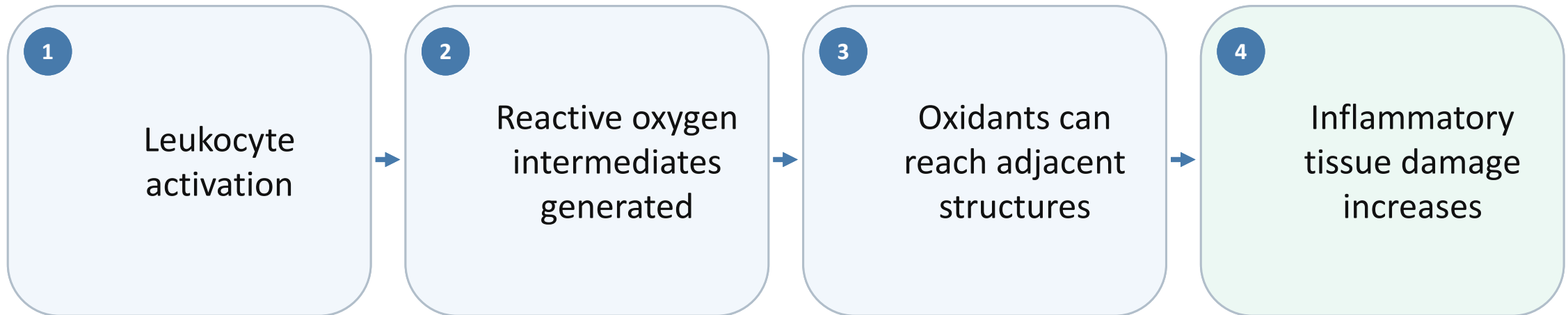
Why enzymes can injure extracellular matrix

Extracellular proteolysis provides a direct mechanism of tissue damage



Reactive oxygen species contribute to tissue injury

Useful antimicrobial chemistry can be harmful when released into tissues



A third type II outcome: Receptor dysfunction

Not all type II reactions remove target cells

Cell depletion

Target cell is physically destroyed

Example: Antibody-mediated blood-cell loss

Receptor dysfunction

Antibody changes receptor signaling/function

Example: Thyroid-stimulating receptor activation in Graves disease

Mechanism selection from the target context

Read the antigen location and endpoint before assigning mechanism

Antibody target	Likely dominant route	Mechanistic endpoint
Mobile cell surface	Opsonin + phagocyte receptor	Cell engulfment and clearance
Susceptible membrane	Terminal complement complex	Osmotic lysis
IgG-coated cell + cytotoxic effector	Fc-mediated ADCC	Killing without ingestion
Fixed tissue matrix	Complement + recruited leukocytes	Inflammatory damage

Clinical reasoning exercise: Incompatible transfusion

A patient receives blood containing erythrocytes with an incompatible antigen.

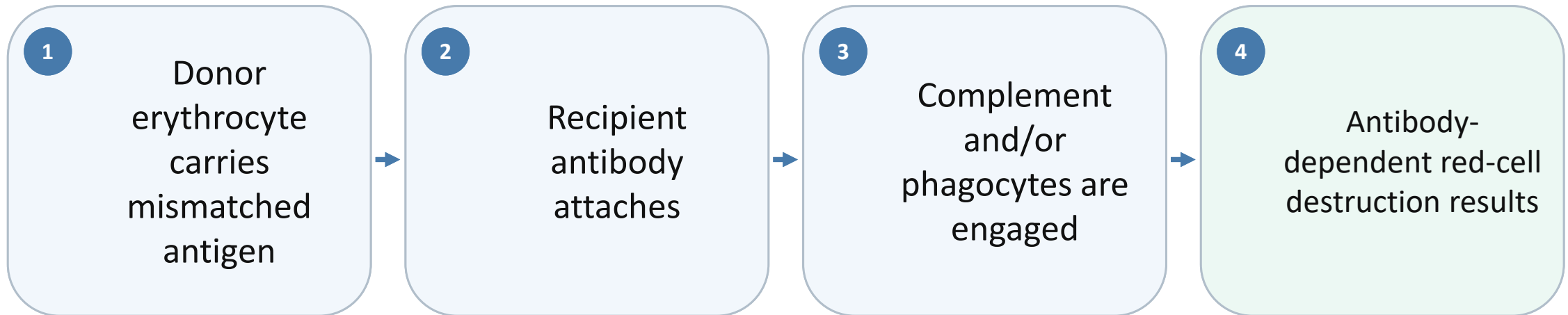
Preformed recipient antibody reacts with those donor cells.

Which target is coated, and how can it be destroyed?

Mechanistic task: Identify target → opsonin → effector

Reasoning: Transfusion incompatibility

The antibody is already present before exposure to the donor target



Clinical reasoning exercise: Fetal anemia

Maternal and fetal erythrocytes differ antigenically.

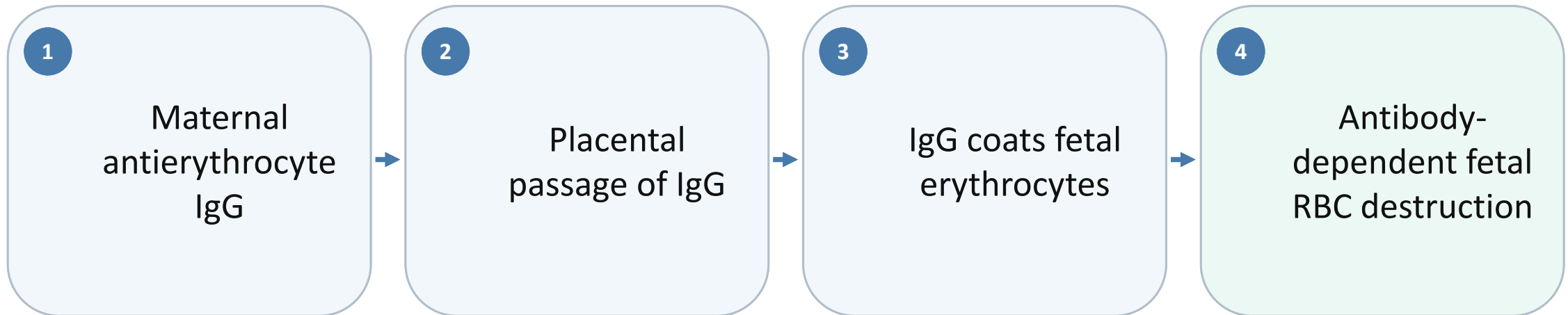
The mother produces antierythrocyte IgG that enters fetal circulation.

What is the causal link between maternal immune response and fetal cell loss?

Mechanistic task: Track compartment crossing before the effector pathway

Reasoning: Transplacental antibody

IgG transfer enables injury across the maternal–fetal interface



Clinical reasoning exercise: Drug-associated cytopenia

A drug binds a membrane-associated protein on circulating blood cells.

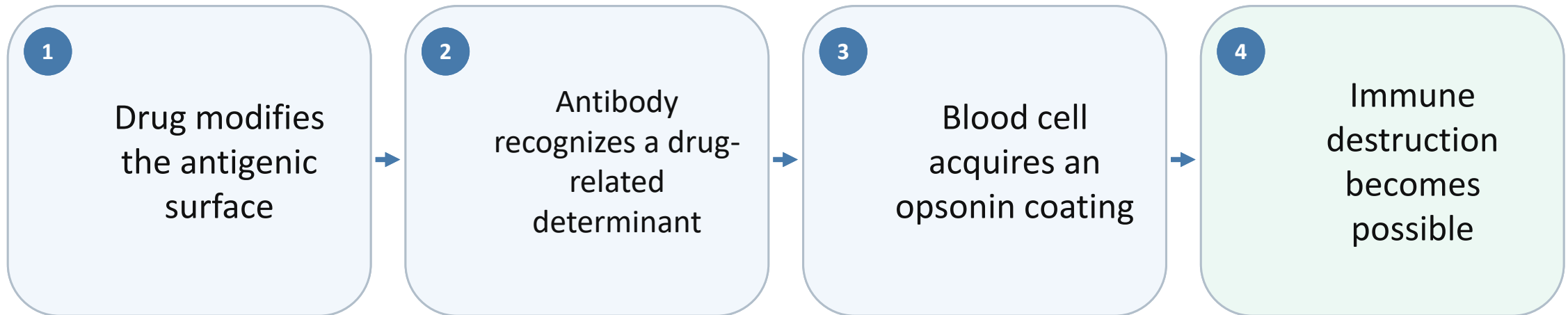
Antibody reactivity emerges toward the drug–protein complex.

Is the antibody necessarily directed against the unchanged native protein?

Mechanistic task: Distinguish an acquired epitope from a constitutive self-antigen

Reasoning: Acquired drug-associated target

An acquired surface determinant can make a host cell vulnerable



Interpretation check: Identify the endpoint

1. C3b on a cell recognized by a phagocyte → ingestion

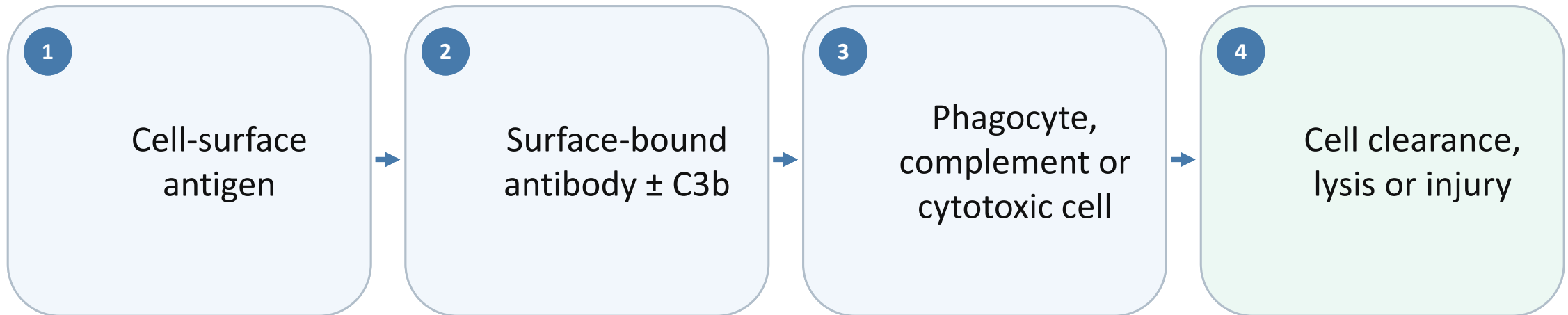
2. MAC disrupts lipid bilayer → osmotic lysis

3. NK cell binds IgG-coated target → killing without uptake

4. Complement at basement membrane → leukocyte-mediated inflammation

Synthesis: Follow antigen → effector → endpoint

An antibody–target interaction is interpreted through its downstream effector



Core mechanisms to retain

- IgG Fc receptors and C3b receptors permit uptake of opsonized cells
- Engulfment and phagolysosomal degradation remove antibody-coated cells
- Terminal complement attack lyses membranes; ADCC kills without ingestion
- Target localization explains the distinction between cytopenia and inflammation

Source reference

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. (2026).
- Chapter 6: Antibody-mediated (type II) hypersensitivity; opsonization and phagocytosis.
- Chapter 3: Phagocytosis and intracellular destruction of microbes and debris.