

Mechanisms of bacterial injury

Virulence, colonization, intracellular persistence and toxins

Attachment

Specific host-cell interactions

Invasion

Intracellular entry and persistence

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Toxins

Direct injury and immune
dysregulation

Learning outcomes

- Relate virulence genes to phenotypic differences between bacterial strains.
- Explain how adherence and biofilms support persistence.
- Compare intracellular entry, survival and host-cell spread.
- Distinguish endotoxin from the major exotoxin mechanisms.

Three principal routes to host injury

Adherence to host cells



Invasion of cells or tissues



Delivery of toxic products

The relative contribution of each route depends on the organism and its virulence determinants.

Virulence reflects a small set of decisive genes

- Many strains of a bacterial species share housekeeping (core) genes.
- Virulence genes encode proteins that enable attachment, entry or toxin delivery.
- Differences in these genes can markedly change the clinical syndrome.

Mechanistic implication

Genetic similarity
does not imply
equivalent
pathogenic
potential.

Salmonella enterica illustrates pathogenic diversity

Closely related isolates

Shared core genome

Single species designation

Overlap in basic cellular functions

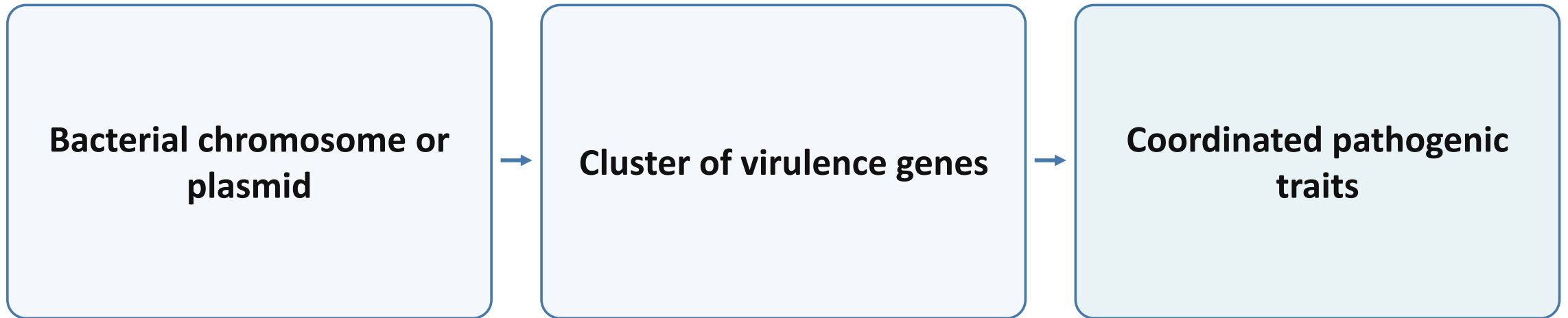
Different clinical consequences

Differences in virulence-gene content

Some isolates produce typhoid fever

Others produce self-limited enteritis

Pathogenicity islands cluster virulence genes



A pathogenicity island is a genomic location, not a distinct class of toxin.

Mobile DNA transfers pathogenic traits

Mobile genetic elements

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graph TD; A[Mobile genetic elements] --> B[Plasmids]; A --> C[Bacteriophages]; A --> D[Bacterial chromosomes]; B --> B1[Resistance and sometimes toxin genes]; C --> C1[Important toxin genes]; D --> D1[Pathogenicity islands];
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Plasmids

Resistance and sometimes toxin genes

Bacteriophages

Important toxin genes

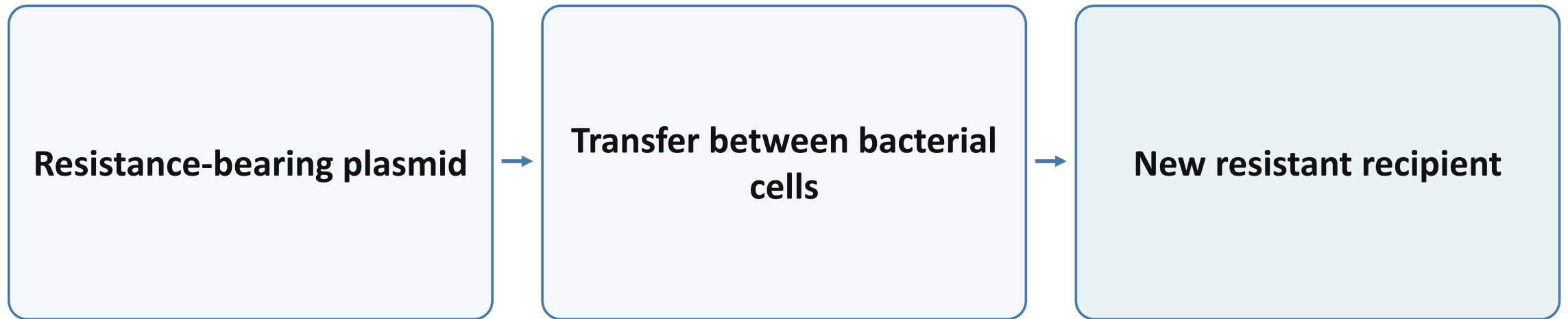
Bacterial chromosomes

Pathogenicity islands

Lysogenic phages can encode major toxins

- Bacteriophages can transfer functionally important genes to bacteria.
- Phage-associated toxin genes in cholera, diphtheria and botulism.
- Acquiring toxin genes can change disease potential without replacing the core genome.

Plasmids are prominent resistance-gene vehicles



Plasmids can spread within a species and across more distantly related organisms.

Vancomycin resistance illustrates cross-species transfer

Original bacterial reservoir

Enterococcus spp.

Mobile plasmid carrying resistance genes

Transferable acquired phenotype

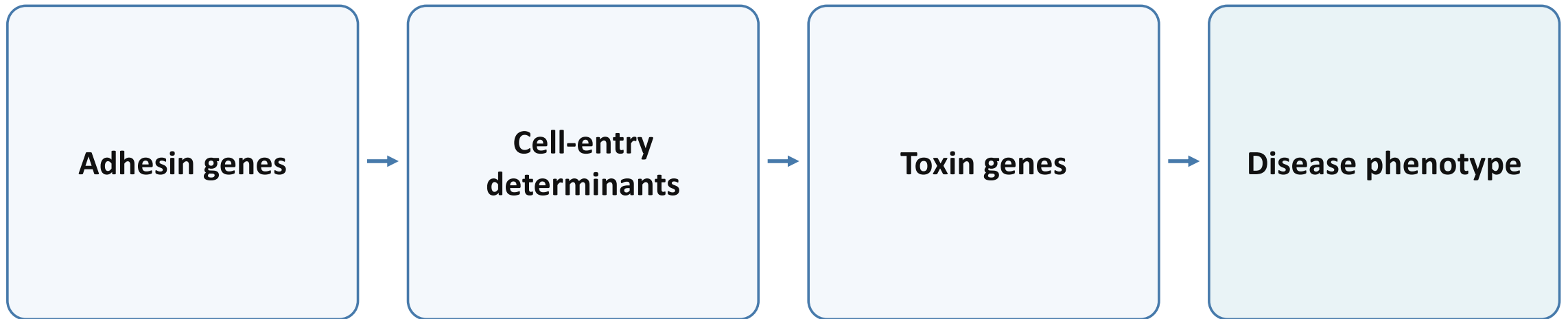
Potential recipient

Staphylococcus aureus

More distantly related organism

Potential acquisition of vancomycin
resistance

Virulence traits are genetically modular



Virulence results from the combination and expression of distinct determinants—not simply bacterial burden.

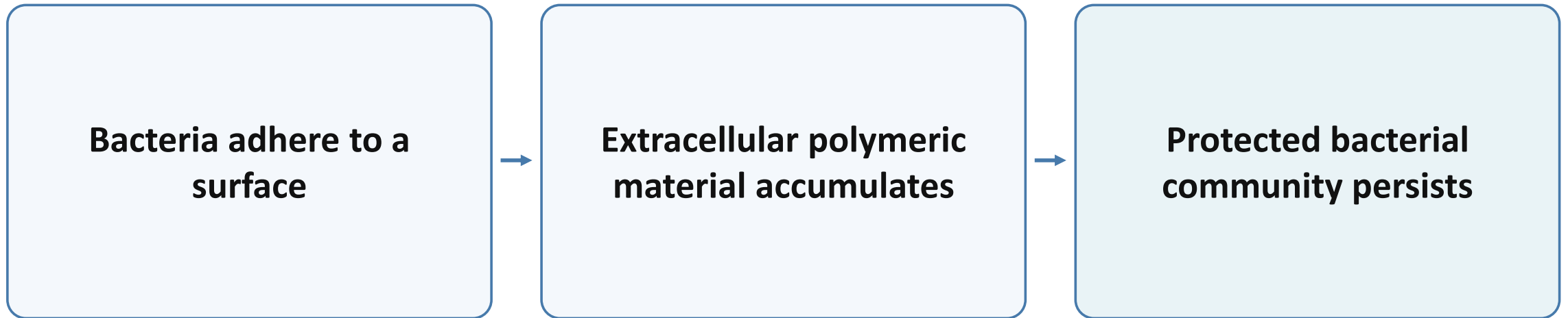
Biofilms are structured bacterial communities

- Organisms reside within an adherent extracellular polymeric matrix.
- The matrix contains polysaccharides, proteins and DNA.
- Biofilms occur on host tissues and implanted devices.

Mechanistic implication

Biofilm = microbial
community plus
protective
extracellular matrix.

Biofilm architecture supports persistence



The schematic describes functional stages; It is not a microscopic image.

Biofilm adhesion prevents easy clearance

- Matrix-associated bacteria remain attached despite mechanical forces.
- Colonization may occur on catheters, prosthetic joints and host tissue.
- Adherence creates an opportunity for continuing local bacterial survival.

Biofilms attenuate host immune clearance

Exposed bacteria

More accessible to immune effectors

Potentially easier to remove mechanically

Bacteria in biofilm

Shielded within polymeric material

Immune effector access and action reduced

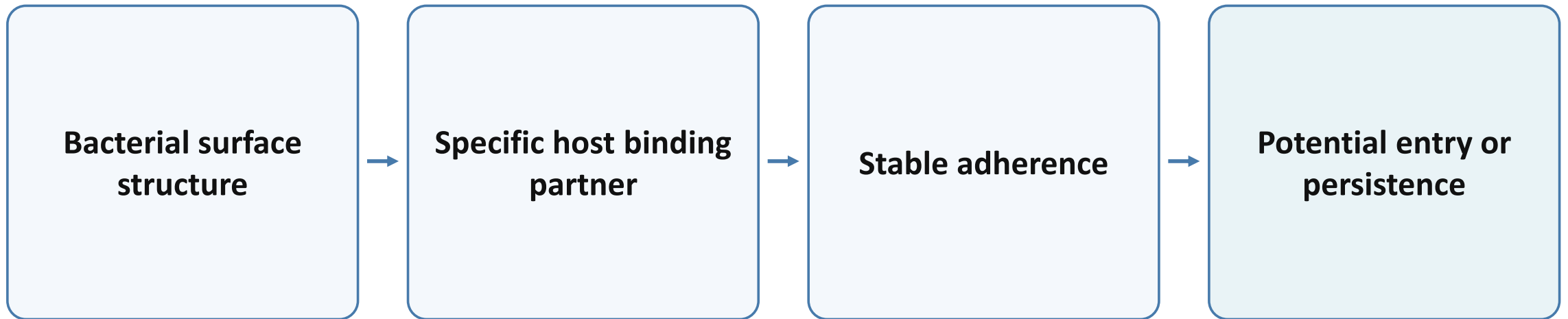
Biofilms increase antimicrobial recalcitrance

- Biofilms with increased resistance to antimicrobial drugs.
- A microbial community can persist even when exposed bacteria are controlled.
- Persistence provides a mechanism for relapse following apparent improvement.

Persistent infection: Characteristic settings

Setting	Role of biofilm
Infective endocarditis	Persistence and relapse
Artificial joint infection	Adherent device-associated bacterial community
Cystic fibrosis respiratory infection	Persistent airway colonization/infection

Adherence is the gateway to colonization



Adhesion counters mechanical removal, including intestinal peristalsis.

Adhesins recognize host-cell and matrix targets

- Adhesins are bacterial surface proteins with host-binding activity.
- Their specificity varies across organisms and host structures.
- Targets can reside on cells or in the extracellular matrix.

Streptococcus pyogenes binds fibronectin



Fibronectin can be present at cell surfaces and within extracellular matrix.

Pili are filamentous adhesion structures

- Pili project from the bacterial surface.
- Stalks comprise repeating conserved protein subunits.
- Variable tip fibrilli contribute tissue-binding specificity.

Mechanistic implication

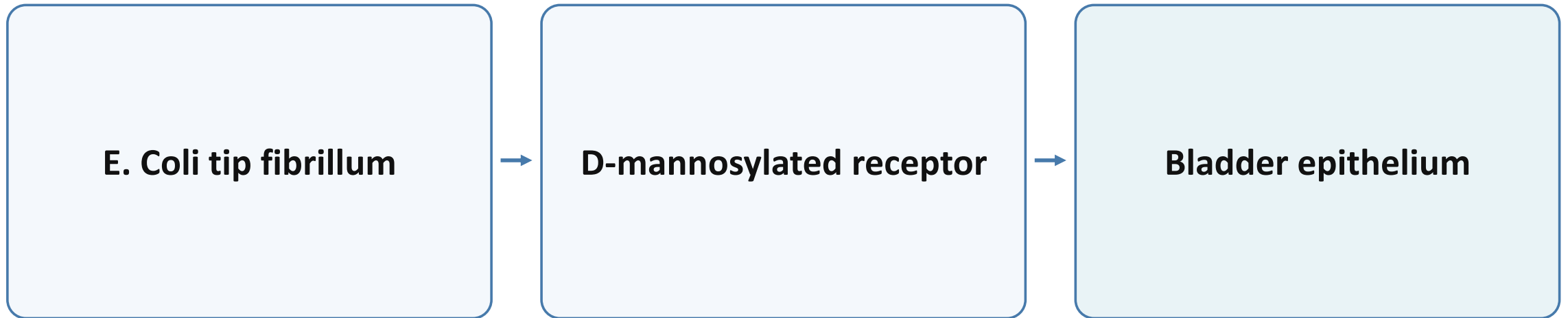
Tip structure—not just presence of a pilus—can determine tropism.

Pilus tips help define tissue tropism



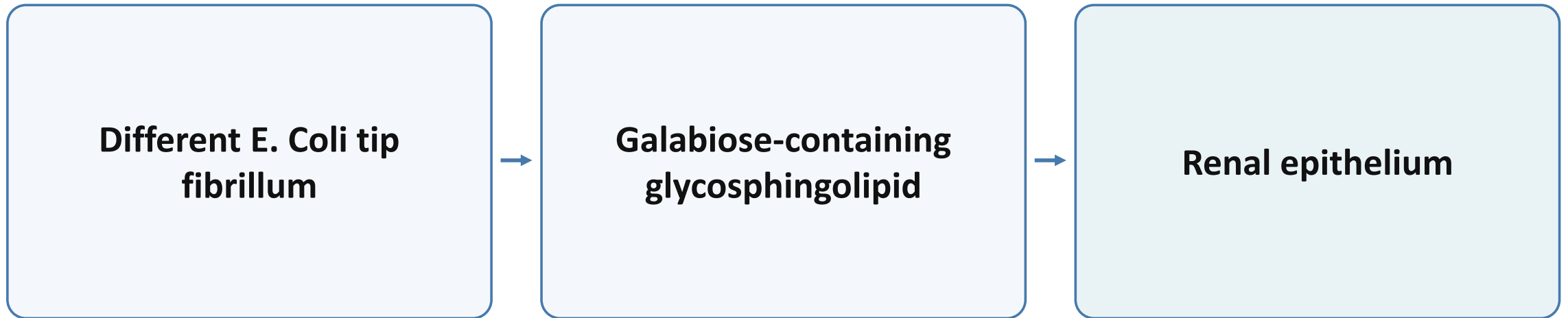
Different tip-binding interactions account for distinct urinary tract sites targeted by E. Coli.

Bladder adhesion: Mannose-containing receptors



This receptor interaction exemplifies organ-specific bacterial binding.

Renal adhesion: Galabiose-containing lipids

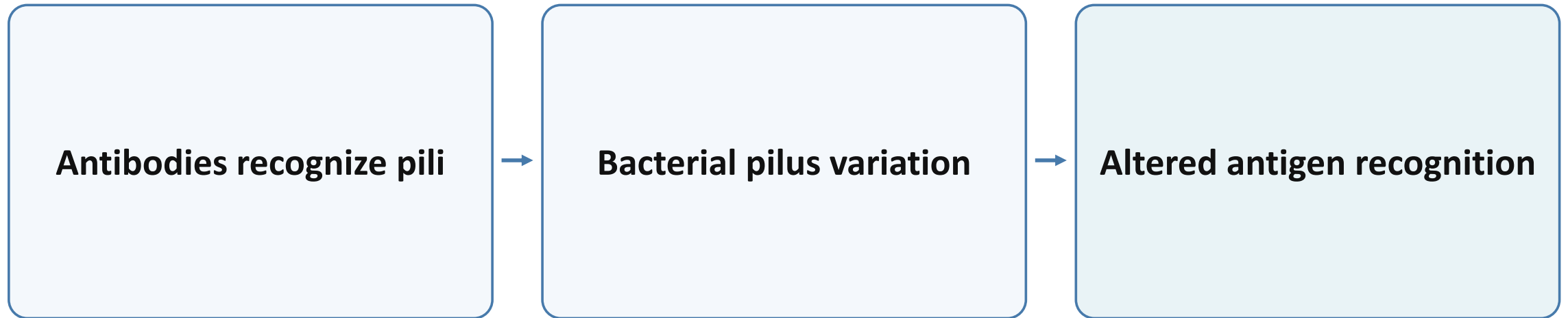


The renal binding specificity differs from the bladder-binding interaction.

One bacterial group, different urinary targets

Tissue	Host binding partner	Bacterial determinant
Bladder epithelium	D-mannosylated receptor	Specific E. coli tip fibrillum
Renal epithelium	Galabiose-containing glycosphingolipid	Different E. coli tip fibrillum

Pilus variation can frustrate immune recognition



Neisseria gonorrhoeae varies its pili as an immune-evasion strategy.

Attachment and evasion can involve one structure

Physical function

Pili bind host targets

Adherence promotes colonization

Site-specific tropism

Immunologic consequence

Pili can be antibody targets

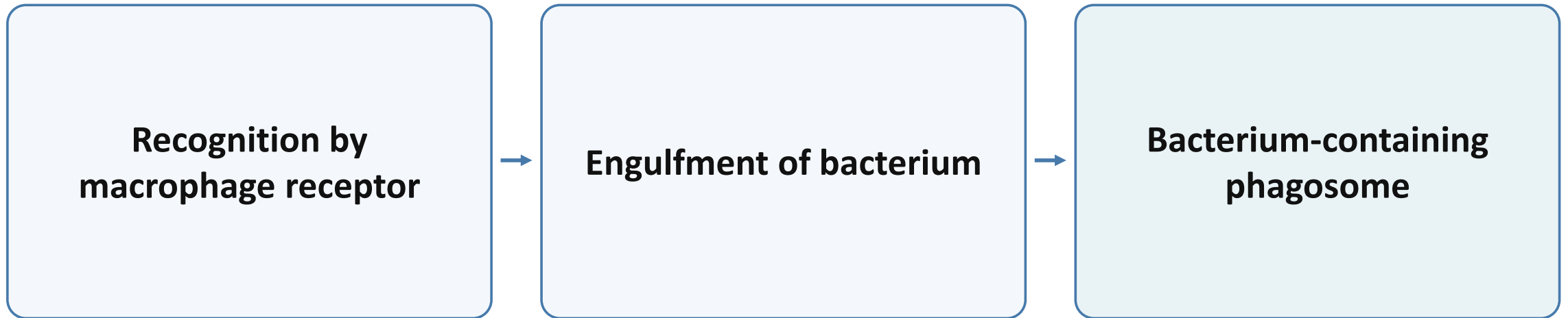
Pilus variation changes antigenicity

Antibody-mediated control may be evaded

Intracellular residence changes the battle

- Intracellular growth can shield bacteria from antibodies and complement.
- Access to host cells depends on organism-specific entry mechanisms.
- Intracellular residence may also facilitate bacterial dissemination.

Macrophage uptake is a possible entry route

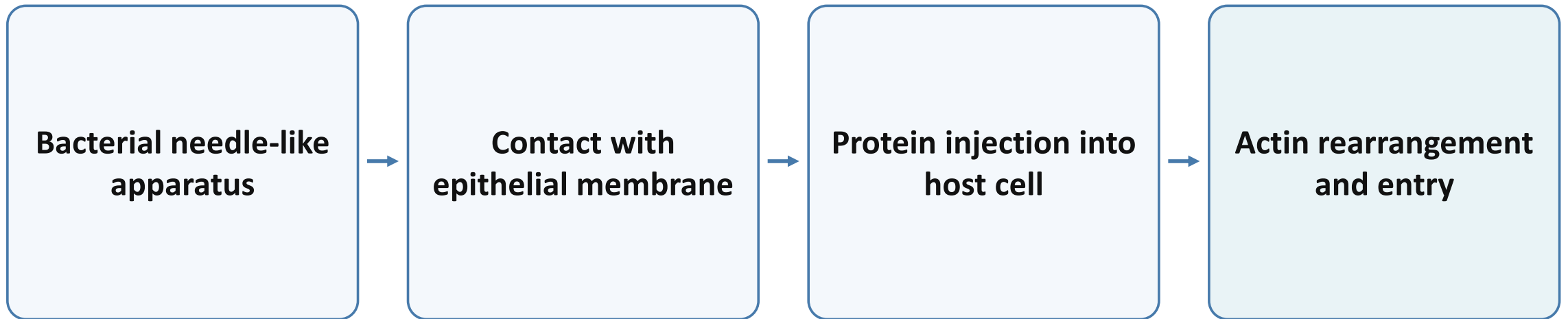


Receptors used in protective immunity can also be exploited by pathogens.

Mycobacterium tuberculosis exploits uptake receptors

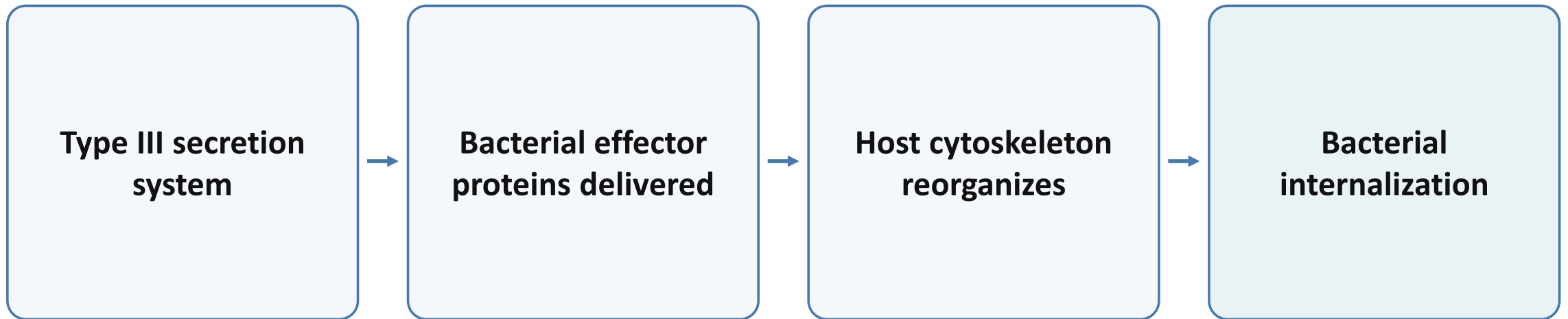
- M. Tuberculosis can use macrophage receptors recognizing opsonins.
- Opsonins named in the source include antibodies and complement C3b.
- Poorly defined nonopsonic receptors can also participate.

Type III secretion enables epithelial entry



A secretion system actively modifies host-cell behavior rather than merely attaching to it.

Injected bacterial proteins remodel actin



The key causal event is host cytoskeletal manipulation.

Salmonella and Shigella use active entry

Shared strategy

Type III secretion apparatus

Needle-like bacterial surface structure

Effector transfer across membrane

Immediate host effect

Host membrane and cytoskeletal alteration

Facilitated epithelial-cell invasion

Intracellular bacterial niche

Internalization is not a uniform outcome

Bacterium enters host cell

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graph TD; A[Bacterium enters host cell] --> B[Killed]; A --> C[Persists]; A --> D[Escapes]; B --> B1[Phagolysosomal digestion]; C --> C1[Avoids normal phagosome maturation]; D --> D1[Moves into host cytoplasm];
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Killed

Phagolysosomal digestion

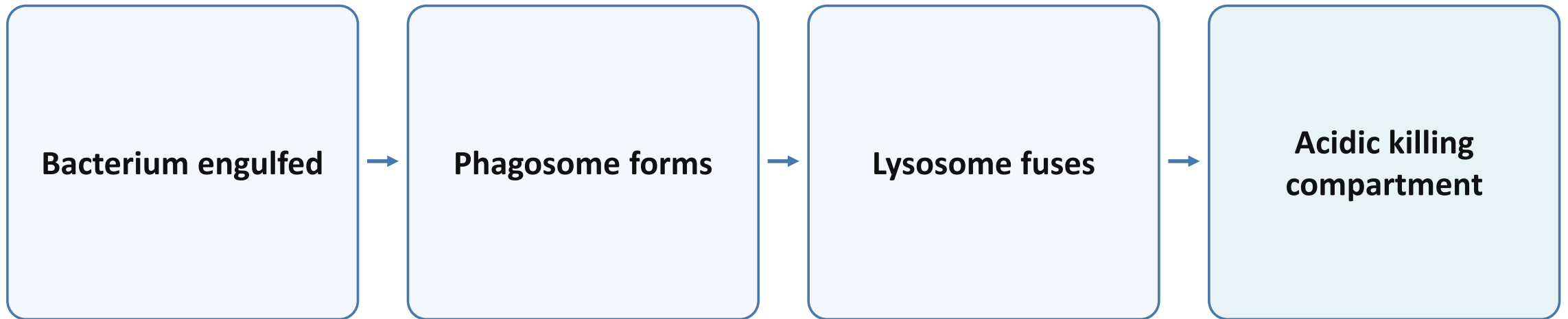
Persists

Avoids normal phagosome
maturation

Escapes

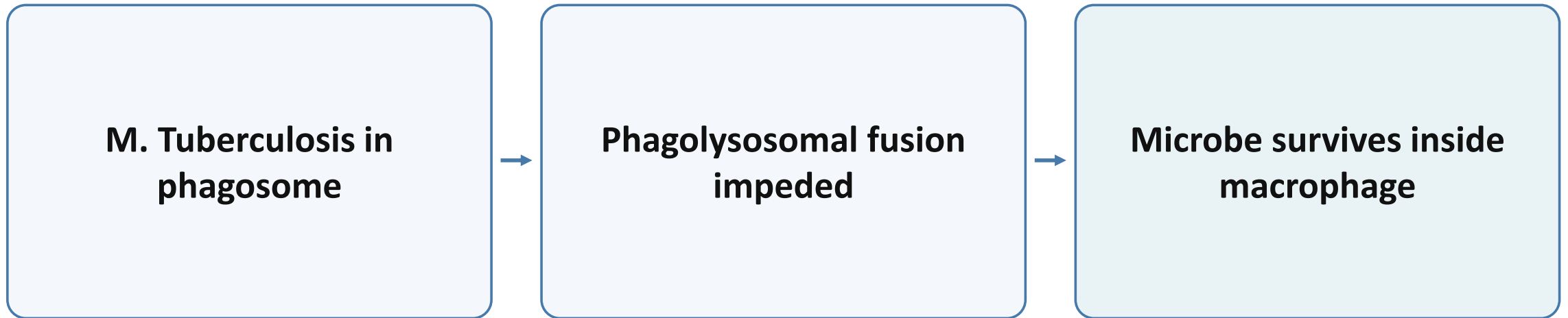
Moves into host cytoplasm

Phagolysosomes normally destroy ingested bacteria



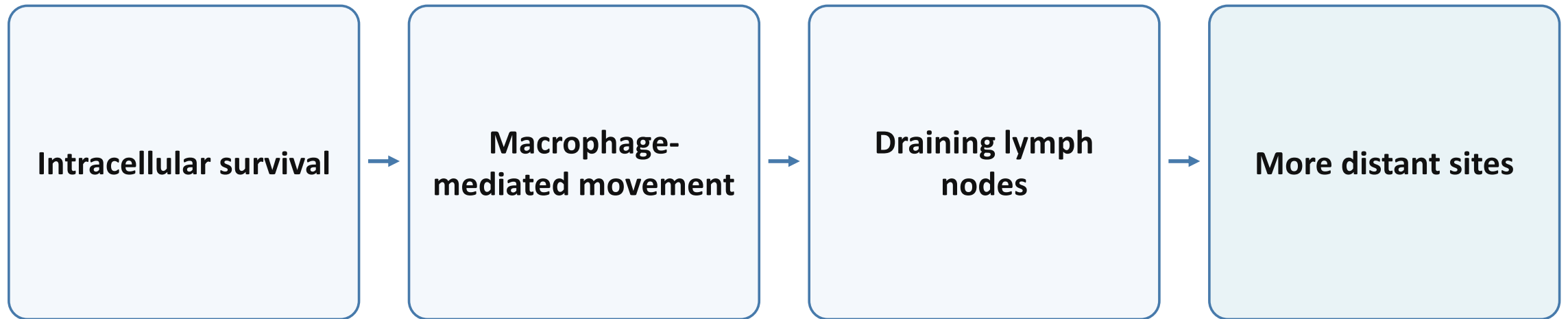
Fusion of phagosomes and lysosomes is a major macrophage bactericidal mechanism.

Tubercle bacilli interrupt phagosome fusion



The main evasion strategy described is blocking phagosome–lysosome fusion.

Infected macrophages can disseminate tuberculosis



Intracellular localization can support transport beyond the initial site.

Listeria uses a different intracellular route

Mycobacterium tuberculosis

Persists in a modified phagosomal compartment

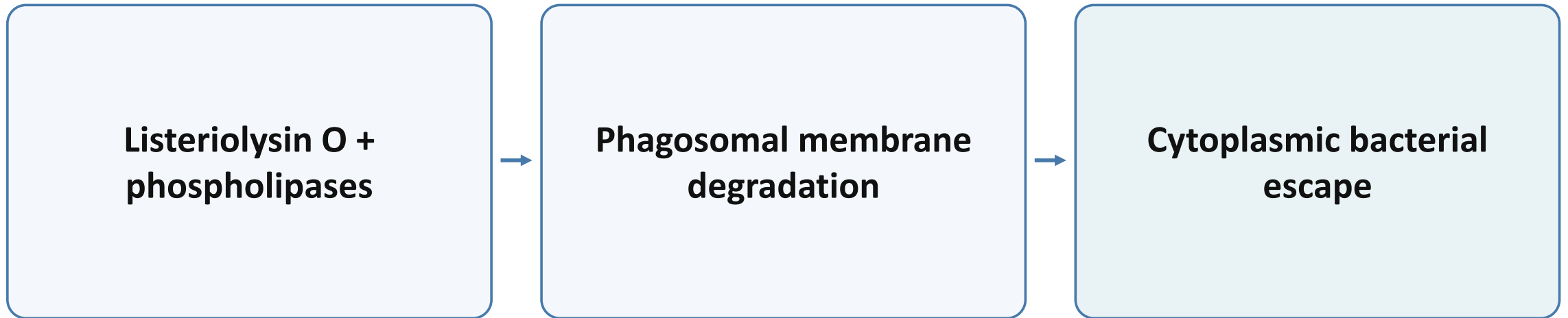
Blocks normal phagosome–lysosome fusion

Listeria monocytogenes

Damages the phagosomal membrane

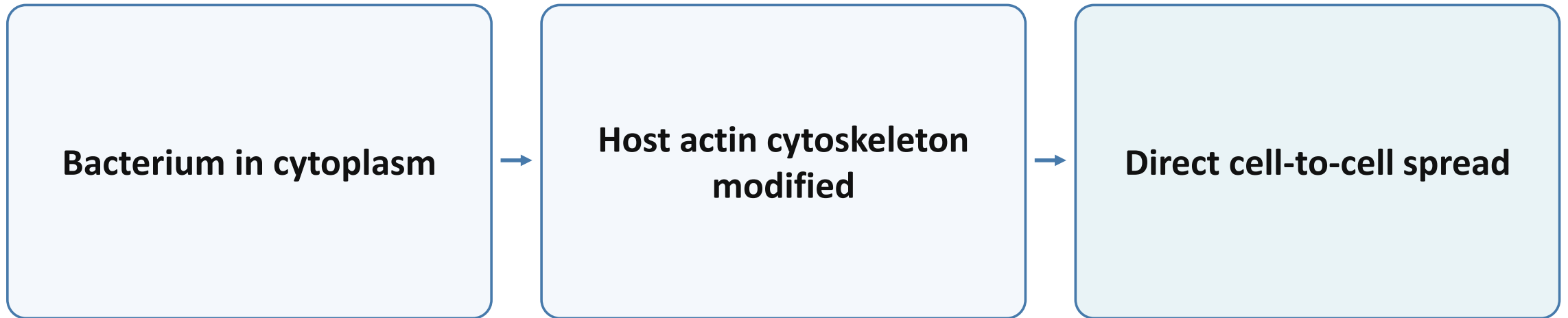
Escapes into the cytoplasm

Listeriolysin O disrupts the phagosomal boundary



A pore-forming toxin and two phospholipases.

Cytoplasmic Listeria spreads directly to neighbors



This route reduces dependence on an extracellular phase.

Some intracellular bacteria rapidly injure cells

- Shigella spp. And E. Coli inhibiting host protein synthesis.
- These bacteria can replicate rapidly after entry.
- The infected host cell may undergo lysis within hours.

Intracellular strategies predict different fates

Pathogen/example	Key host manipulation	Result
M. tuberculosis	Blocks phagolysosomal fusion	Macrophage persistence
L. monocytogenes	Disrupts phagosome; exploits actin	Cytoplasmic spread
Shigella / E. coli	Inhibit host protein synthesis	Rapid lytic injury

Bacterial toxins: Two broad categories

Endotoxin

Component of Gram-negative outer membrane

Lipopolysaccharide (LPS)

Activates host inflammatory responses

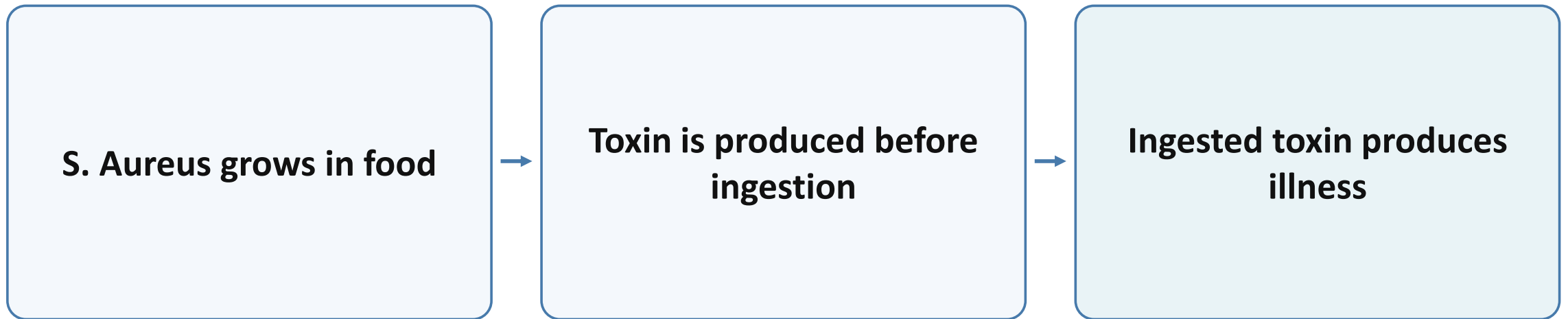
Exotoxin

Protein secreted by many bacteria

Enzymatic or signaling effects

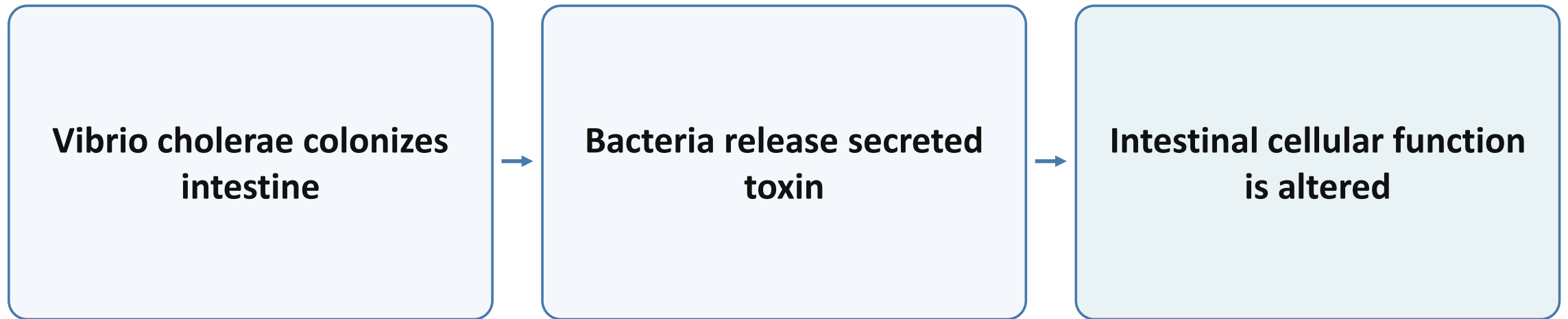
Can injure cells independent of ongoing infection

Toxin exposure does not require live infection



Preformed toxin exposure illustrates intoxication rather than the necessity of host colonization.

Other toxins are generated within the host

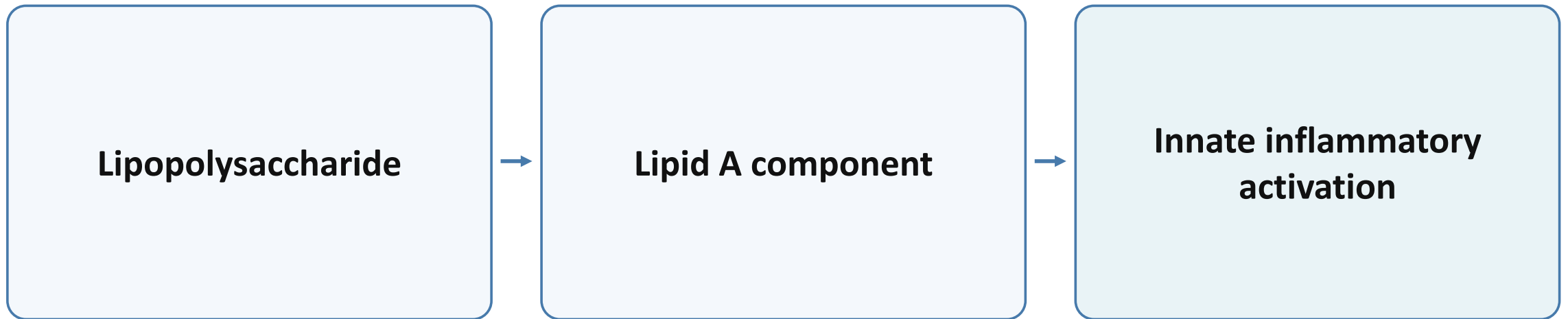


An organism can remain at a mucosal surface while its toxin drives disease.

Endotoxin is part of Gram-negative LPS

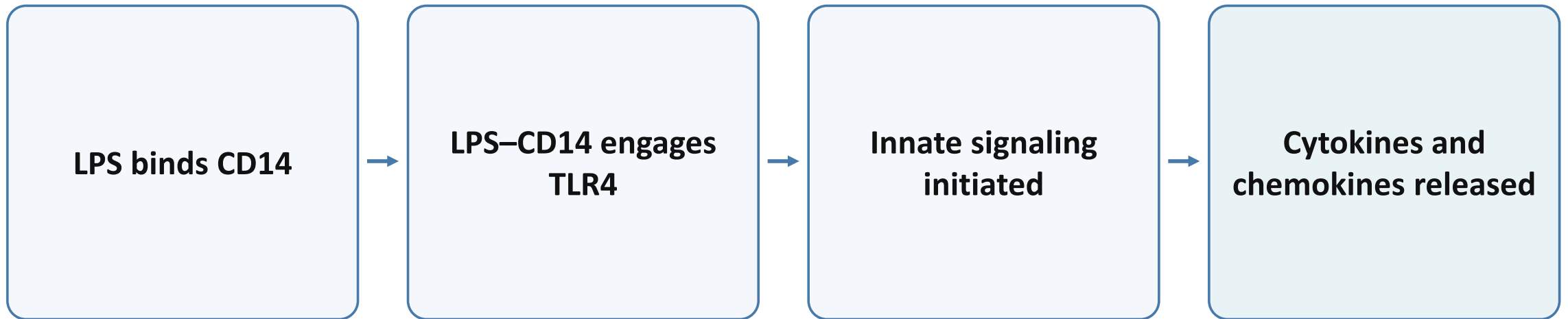
- LPS resides in the outer membrane of Gram-negative bacteria.
- Its presence is detected by innate immune receptors.
- LPS can both activate protective immunity and cause systemic injury.

Lipid A carries the endotoxin activity



Lipid A is the membrane-anchoring portion responsible for LPS endotoxin effects.

CD14 and TLR4 detect LPS



The source describes CD14 as soluble or cell-associated.

Gram-positive structures can trigger related signals

Gram-negative bacteria

Lipopolysaccharide

Endotoxic activity associated with lipid A

CD14 → TLR4 response

Gram-positive bacteria

Lipoteichoic acid

Inflammatory activities resembling
endotoxin

TLR2 response

Innate activation is initially protective

Recognition of bacterial products

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graph TD; A[Recognition of bacterial products] --> B[Cytokines  
Coordinate antimicrobial response]; A --> C[Chemokines  
Recruit effector cells]; A --> D[Costimulation  
Supports T-cell activation];
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Cytokines

Coordinate antimicrobial response

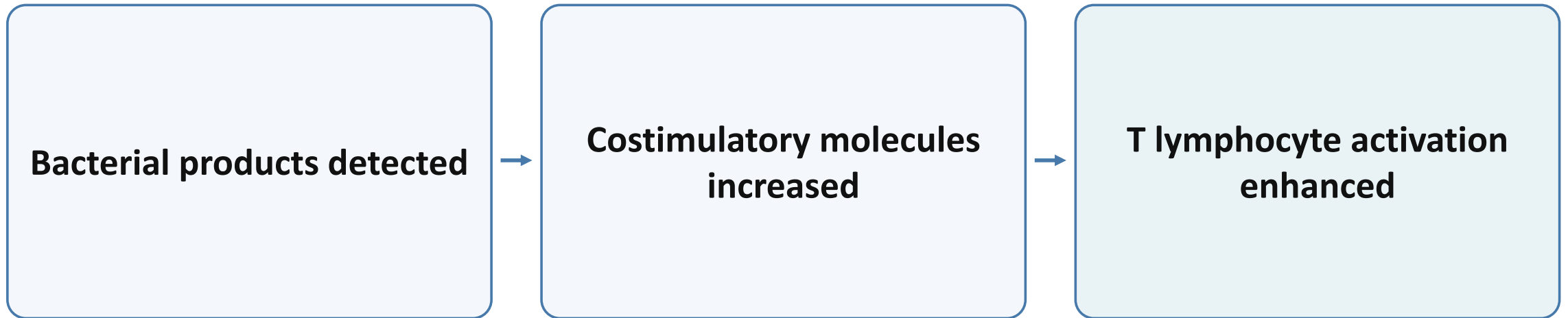
Chemokines

Recruit effector cells

Costimulation

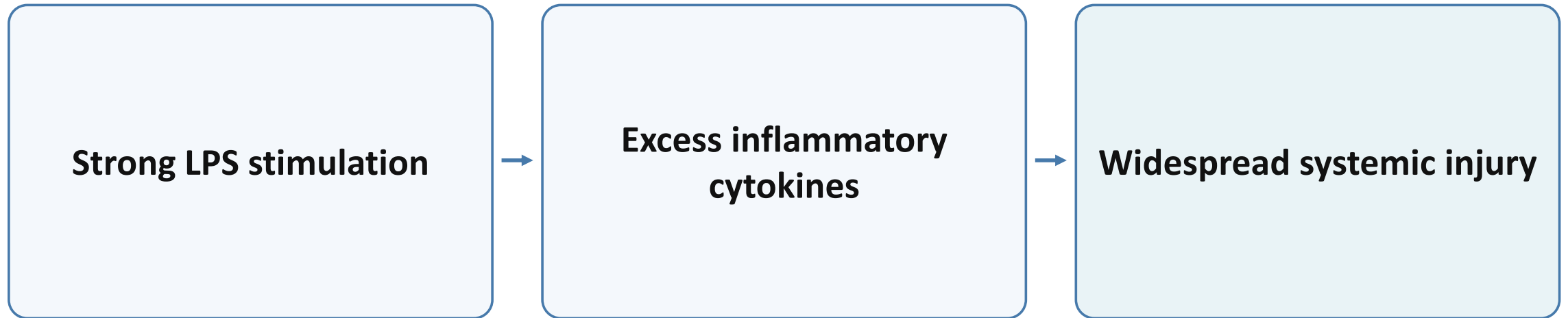
Supports T-cell activation

Costimulation connects innate to adaptive defense



Innate recognition shapes subsequent adaptive immune responses.

High endotoxin exposure drives cytokine excess



TNF, IL-6 and IL-12 are specifically identified in the source.

Endotoxin can precipitate life-threatening syndromes

**Excess systemic inflammatory
activation**

Septic shock

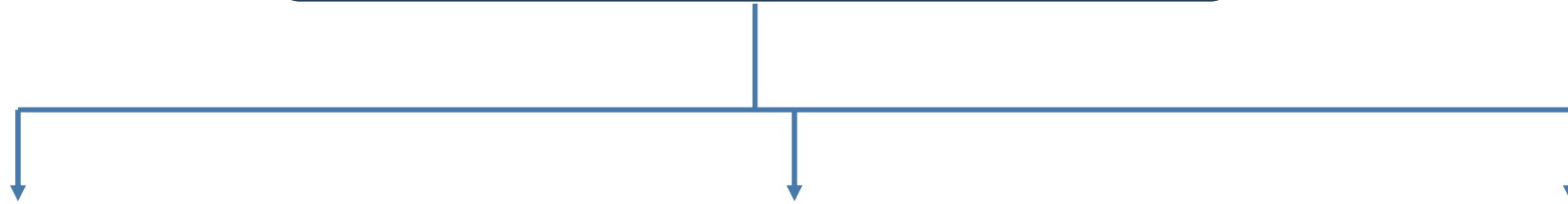
Circulatory dysfunction

DIC

Disseminated coagulation

ARDS

Acute lung injury



One LPS signal: Protection or pathology

Controlled response

Cytokines and chemokines support defense

Costimulation improves T-cell activation

Local immune coordination

Excessive response

Excessive cytokine release

Septic shock and DIC

Acute respiratory distress syndrome

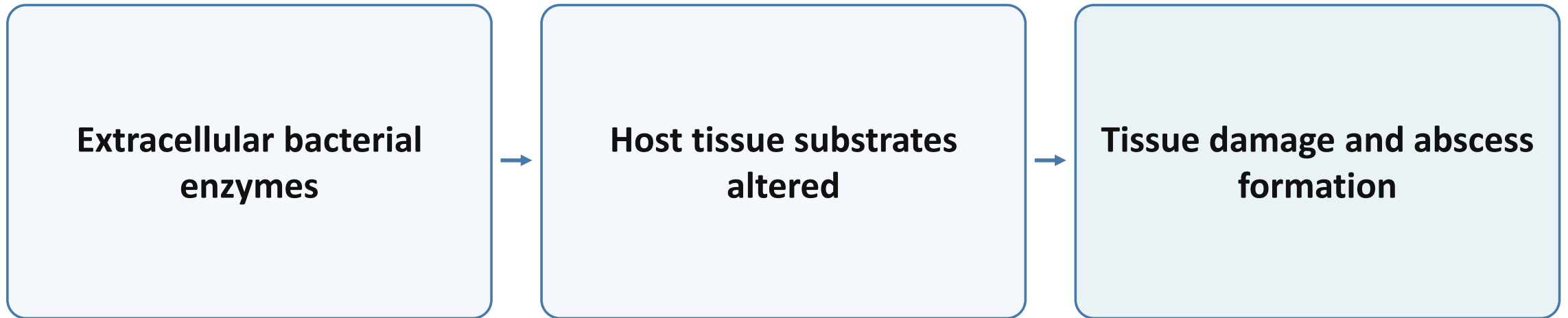
Exotoxins are secreted bacterial proteins

- Exotoxins directly alter host tissues or cellular functions.
- Their actions differ according to binding targets and enzymatic activity.
- Robbins groups them as tissue-active enzymes, pathway-altering toxins, and superantigens.

Secreted enzymes alter host tissues

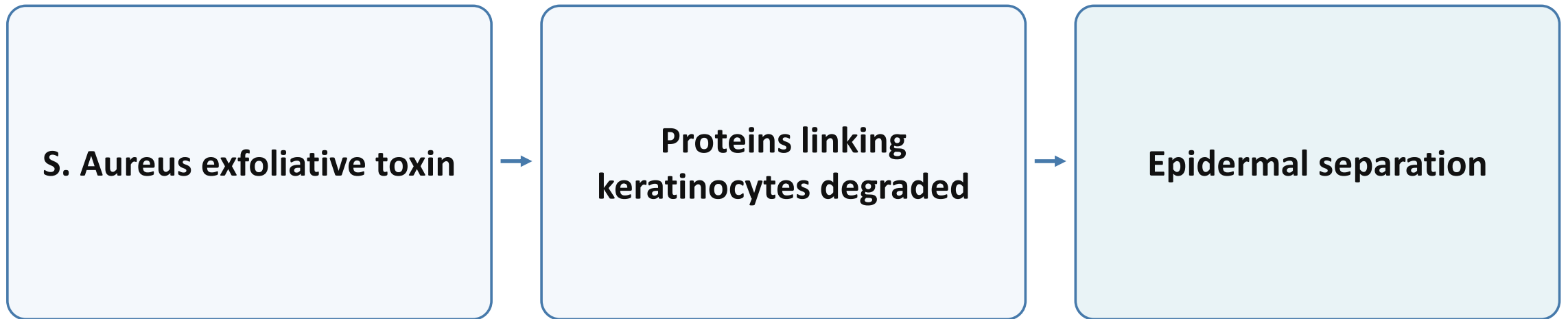
Enzyme family	Mechanistic description
Proteases	Degrade protein substrates
Hyaluronidases	Act on tissue matrix components
Coagulases / fibrinolysins	Influence clot-related substrates

Bacterial enzymes contribute to local destruction



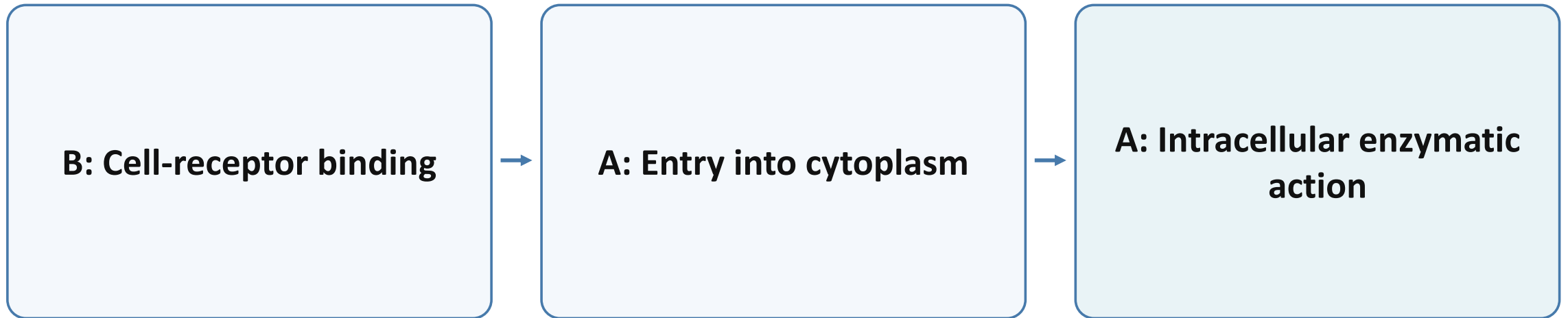
Enzyme action provides one causal link between infection and local destructive morphology.

Exfoliative toxins disrupt epidermal adhesion



The clinical correlate is staphylococcal scalded-skin syndrome.

Many toxins have A and B functional domains



Binding specificity determines target-cell access; Catalytic activity determines the disrupted pathway.

A–B toxin effects vary with target and enzyme

Binding component (B)

Engages an appropriate surface receptor

Helps deliver toxin into the cell

Contributes target-cell specificity

Active component (A)

Carries enzymatic activity

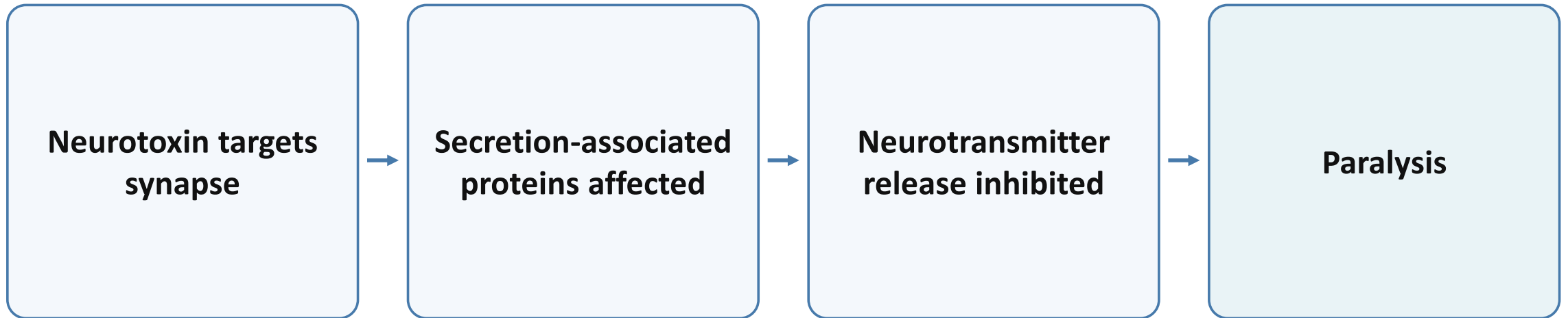
Acts on an intracellular pathway

Produces functional injury

A–B toxins occur in several bacterial diseases

Bacterial example	Source-supported point
Bacillus anthracis	Produces A–B toxins
Vibrio cholerae	Produces an A–B toxin
Some E. coli strains	Produce A–B toxins
Clostridium botulinum / C. tetani	A–B neurotoxins affect neurotransmitter release

Clostridial neurotoxins inhibit transmitter release



Neuron death is not required to produce profound neuromuscular dysfunction.

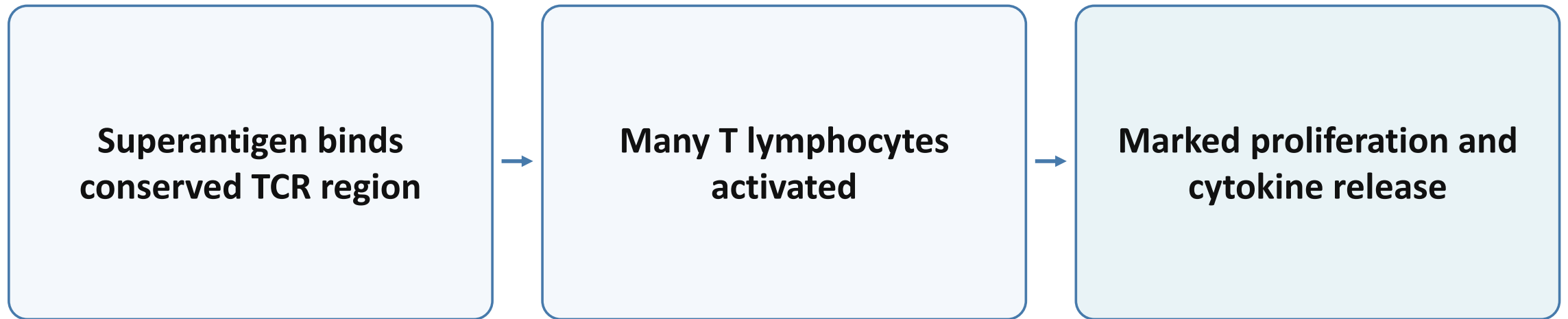
Paralysis can cause respiratory failure

- Tetanus and botulism are neurotoxin-mediated diseases.
- Paralysis can impair movement of chest wall and diaphragm muscles.
- Loss of respiratory muscle function can be fatal.

Mechanistic implication

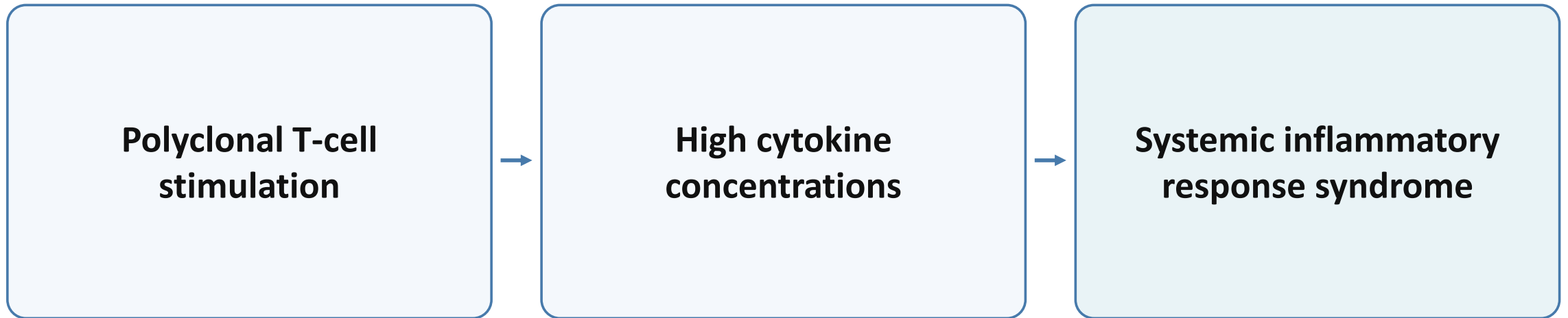
Functional synaptic blockade must not be equated with death of the neuron.

Superantigens activate large T-cell populations



Superantigen activation differs from ordinary narrowly specific antigen recognition.

Superantigen injury is cytokine mediated



Host immune activation becomes the proximate cause of widespread injury.

Three exotoxin mechanisms compared

Exotoxin class	Primary target/process	Characteristic consequence
Tissue-active enzymes	Extracellular host substrates	Destruction / altered tissue cohesion
A–B toxins	Specific intracellular pathways	Cell dysfunction; paralysis in neurotoxin examples
Superantigens	Broad T-lymphocyte activation	Excessive cytokine release

Clinical problem: Urinary epithelial tropism

Two E. Coli isolates display different affinity for bladder and renal epithelium. Which bacterial structure best explains their different tissue targets?

Evidence to interpret

- A surface filament is present in both organisms.
- Host cell binding receptors differ by tissue.

Mechanism: Variation in pilus tip fibrils changes receptor specificity.

Clinical problem: Relapsing device infection

An intravascular catheter infection repeatedly recurs despite an initial clinical response. What bacterial organization could account for persistence?

Evidence to interpret

- Organisms remain associated with the device surface.
- Host defenses and antimicrobials have difficulty clearing the community.

Mechanism: An adherent biofilm embedded in extracellular polymeric substances.

Clinical problem: Intracellular survival

**A pathogen survives in macrophages by preventing phagosome–lysosome fusion.
Which organism and strategy are represented?**

Evidence to interpret

- The organism enters through macrophage uptake pathways.
- The normal acidified killing compartment does not form.

Mechanism: *Mycobacterium tuberculosis*—interference with phagolysosomal fusion.

Clinical problem: Paralysis without neuron death

A bacterial toxin produces paralysis by inhibiting neurotransmitter secretion, without requiring neuron destruction. What toxin architecture and target process explain this?

Evidence to interpret

- A receptor-binding component delivers an active component.
- Synaptic exocytosis-associated proteins are affected.

Mechanism: A–B clostridial neurotoxin acting on neurotransmitter-release machinery.

Unifying scheme: Bacterial injury is multilevel

Microbial virulence determinants

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graph TD; A[Microbial virulence determinants] --> B[Surface interaction<br/>Adherence and biofilm persistence]; A --> C[Cellular entry<br/>Intracellular survival or lysis]; A --> D[Secreted / structural products<br/>Direct toxicity and immune overactivation];
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Surface interaction

Adherence and biofilm
persistence

Cellular entry

Intracellular survival or lysis

Secreted / structural products

Direct toxicity and immune
overactivation

Mechanistic distinctions to retain

Question	Preferred mechanistic answer
Why does a bacterium adhere?	Adhesin / pilus interaction with specific host targets
Why can infection recur on a device?	Biofilm matrix protects attached organisms
Why can macrophages harbor bacteria?	Blocked phagolysosomal fusion or escape
Why can toxins injure systemically?	Direct pathway disruption or disproportionate cytokine response

Reference and source boundary

Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th ed. (2026). Chapter 8, “Mechanisms of Bacterial Injury,” printed pp. 309–311.

Source: supplied project Markdown extraction and teaching-unit file. Original chapter PDF and Figure 8.4 were not supplied; diagrams in this lecture are original editable schematics, not reproductions of the textbook figure.

No additional external scientific sources were used.