

# Innate Immunity: Physical and Mechanical Barriers

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## Abstract

Innate immunity constitutes the first line of host defense against invading pathogens (Turvey & Broide, 2010). Among its components, physical and mechanical barriers play a fundamental role by preventing microbial entry, colonization, and dissemination. This educational note provides a comprehensive overview of these barriers across different anatomical sites, including the skin, mucous membranes, respiratory tract, gastrointestinal tract, genitourinary tract, and eyes. It also details associated chemical factors (e.g., lysozyme, lactoferrin, gastric juice, bacteriocins) and cellular elements such as Langerhans cells, M cells, and alveolar macrophages (Abbas et al., 2020; Gallo & Hooper, 2012). The note emphasizes the synergistic action of physical, mechanical, and chemical mechanisms that together form an effective surveillance system. Understanding these barriers is essential for appreciating how the body resists infection before adaptive immunity is engaged.

## Keywords:

: Innate immunity, physical barriers, mechanical barriers, skin, mucous membranes, lysozyme, lactoferrin, M cells, alveolar macrophages, SALT, mucosal-associated lymphoid tissue, antimicrobial peptides

## Introduction to Innate Immunity

Innate immunity is the evolutionarily ancient, non-specific defense system that responds immediately to pathogens. Unlike adaptive immunity, it does not require prior exposure and lacks immunological memory (Turvey & Broide, 2010). The physical and mechanical barriers are the most external components of innate immunity, designed to **prevent pathogen entry** or **rapidly remove** them before infection can establish (Abbas et al., 2020).

These barriers include:

- Intact skin and mucous membranes.
- Mechanical actions such as shedding, flushing, ciliary movement, peristalsis, coughing, and sneezing.
- Chemical factors that directly kill or inhibit microbes (Gallo & Hooper, 2012).

Together, they provide a formidable first line of defense.

### 1. The Skin: A Multilayered Physical and Chemical Fortress

The skin is the largest organ of the body ( $\approx 1.5\text{--}2\text{ m}^2$ ) and serves as a primary physical barrier (Nestle et al., 2009).

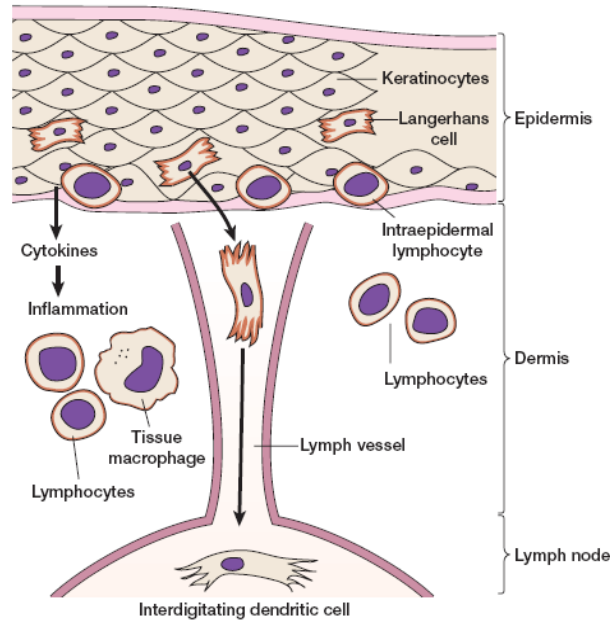
#### 1.1 Structural Features

- **Keratinocytes** form multiple layers of stratified squamous epithelium; the outer layer (stratum corneum) is composed of dead, keratin-filled cells that are impermeable to most microorganisms (Nestle et al., 2009).
- **Continuous shedding** of outer epithelial cells removes attached microbes (Abbas et al., 2020).
- **Relative dryness** (low water activity) slows microbial growth (Gallo & Hooper, 2012).
- **Mild acidity** (pH 5–6) – due to lactic acid, free fatty acids, and amino acids – inhibits many pathogenic bacteria and fungi (Schroder, 2011).
- **Sebum** (from sebaceous glands) contains triglycerides that are broken down into free fatty acids with antimicrobial activity (Schroder, 2011).
- **Normal skin microbiota** (e.g., *Staphylococcus epidermidis*) produces bacteriocins and competes for nutrients, antagonizing pathogens like *Staphylococcus aureus* (Gallo & Hooper, 2012).
- **Hygiene** (washing) mechanically removes transient microorganisms.

#### 1.2 Skin-Associated Lymphoid Tissue (SALT)

The skin is not just a passive barrier; it contains specialized immune cells (Nestle et al., 2009):

- **Langerhans cells** – dendritic cells in the epidermis that phagocytose antigens, migrate to draining lymph nodes, mature into interdigitating dendritic cells, and present antigens to naïve T cells, initiating adaptive immunity (Abbas et al., 2020).
- **Intraepidermal lymphocytes** – primarily  $\gamma\delta$  T cells that act like cytotoxic T lymphocytes, destroying infected keratinocytes (Nestle et al., 2009).
- **Large numbers of macrophages** in the dermis that phagocytose pathogens and produce inflammatory cytokines (Abbas et al., 2020).



## 2. Mucous Membranes and Mucosal-Associated Lymphoid Tissue (MALT)

Mucous membranes line internal cavities exposed to the external environment (oral cavity, nasal passages, gut, vagina, etc.). They are more delicate than skin but have specialized defenses (Mestecky et al., 2015).

### 2.1 General Features

- **Mucus** – a viscous secretion containing glycoproteins (mucins) that traps microorganisms (Mestecky et al., 2015).
- **Antimicrobial components:**
  - **Cervical mucus** – impedes ascent of bacteria into the uterus.
  - **Prostatic fluid** – contains zinc and antibacterial factors.
  - **Tears** – contain lysozyme, lactoferrin, and sIgA (Kolar & McDermott, 2019).

### 2.2 M Cells (Microfold Cells)

M cells are specialized epithelial cells found overlying lymphoid follicles in the gut, tonsils, and Peyer's patches (Mestecky et al., 2015).

- **Structure:** Lack microvilli (brush border) but have a pocket on their basolateral side containing B cells, T cells, and macrophages (Abbas et al., 2020).
- **Function:**
  1. Phagocytose antigens and pathogens from the gut lumen.
  2. Transport them across the epithelial barrier into the pocket.
  3. Macrophages in the pocket engulf the antigen.
  4. Alternatively, M cells deliver antigens to organized lymphoid follicles.
  5. B cells in the follicle recognize the antigen, mature into plasma cells, and secrete **secretory IgA (sIgA)** (Mestecky et al., 2015).
  6. sIgA is transported into the gut lumen to neutralize specific pathogens.

This mechanism is a critical bridge between innate and adaptive immunity at mucosal surfaces (Abbas et al., 2020).



- Production of **bacteriocins** (e.g., colicin from *E. coli*, staphylococcin from *Staphylococcus*) (Gallo & Hooper, 2012).
- Competition for nutrients and adhesion sites.
- Stimulation of host immune responses (Mestecky et al., 2015).

## 5. Genitourinary Tract Defenses

The urinary and reproductive tracts are protected by several features (Abbas et al., 2020):

- **Urine properties:** Low pH ( $\approx 5.5-6.5$ ), high urea concentration, uric acid, and hippuric acid – all inhibit microbial growth.
- **Hypotonic effect** of the kidney medulla – creates osmotic stress for bacteria.
- **Flushing action** – frequent voiding of urine mechanically removes pathogens.
- **Distance barrier** – long urethra ( $\approx 20$  cm in males) makes ascending infection more difficult.
- **Secretory antibodies (sIgA)** in cervical mucus neutralize sperm-borne and sexually transmitted pathogens (Mestecky et al., 2015).
- **Prostatic antibacterial factor** – a zinc-containing peptide with antimicrobial activity.

## 6. The Eyes: Continuous Cleansing

The ocular surface is constantly exposed but remains remarkably infection-free due to (Kolar & McDermott, 2019):

- **Continuous flushing** by tears (produced by lacrimal glands, drained via nasolacrimal duct).
- **Tear composition:**
  - **Lysozyme** (muramidase) – breaks the  $\beta(1\rightarrow4)$  bond between N-acetylmuramic acid and N-acetylglucosamine in peptidoglycan, especially effective against Gram-positive bacteria (Kolar & McDermott, 2019).
  - **Lactoferrin** – iron-binding protein that sequesters iron, limiting bacterial growth (Kolar & McDermott, 2019).
  - **sIgA** – neutralizes pathogens and prevents adhesion (Mestecky et al., 2015).
  - **Lactoperoxidase** – generates superoxide radicals that kill microbes.

Thus, tears provide both physical (flushing) and chemical protection.

## 7. Chemical Barriers: A Closer Look

While many chemical factors are associated with specific sites, some are systemic or widely distributed (Gallo & Hooper, 2012; Schroder, 2011).

Chemical Barrier	Source	Mechanism of Action
Lysozyme	Tears, saliva, mucus, milk	Hydrolyzes peptidoglycan (Gram-positive bacteria) (Kolar & McDermott, 2019)
Lactoferrin	Neutrophils, macrophages, secretions	Iron chelation; disrupts bacterial membranes (Kolar & McDermott, 2019)
Lactoperoxidase	Saliva, milk, tears	Generates hypothiocyanite and superoxide radicals
Gastric juice	Stomach	Acid denaturation of proteins (Abbas et al., 2020)
Salivary glycoproteins	Saliva	Inhibit bacterial adhesion
Urea	Urine	Alkaline degradation products are antimicrobial
Bacteriocins (colicin, staphylococcin)	Commensal bacteria	Pore formation, cell wall synthesis inhibition (Gallo & Hooper, 2012)
$\beta$ -Lysin	Blood platelets	Disrupts microbial plasma membrane
Leukins	Neutrophils	Cationic antimicrobial peptides (Schroder, 2011)
Phagocytin	Phagocytes	Antimicrobial protein
Prostatic antibacterial factor	Prostate fluid	Zinc-dependent antimicrobial activity

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## 8. Summary and Clinical Relevance

- Physical and mechanical barriers are the first and most immediate components of innate immunity (Turvey & Broide, 2010).
- They act by **blocking entry** (skin, mucous membranes), **removing microbes** (shedding, cilia, flushing, peristalsis), and **killing** (chemicals, phagocytes) (Abbas et al., 2020).
- These barriers are not passive; they include specialized immune cells (Langerhans cells, M cells, alveolar macrophages) that initiate adaptive responses when breached (Nestle et al., 2009; Sarkar & Tindle, 2021).
- **Defects in these barriers** predispose to infection: e.g., burns (loss of skin barrier), cystic fibrosis (impaired mucociliary clearance), gastric acid suppression (increased risk of GI infections) (Gallo & Hooper, 2012).

Understanding these mechanisms is crucial for developing strategies to prevent infections and for appreciating how the body maintains homeostasis with the microbial world.

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### Data Availability Statement

No original datasets were generated for this review article. All cited data and findings are available within the original research publications referenced in the manuscript, accessible via the provided Digital Object Identifiers (DOIs) or through respective journal platforms.