

**Subject: Physiology of Coordination
(BS Zoology 6th Semester)**

Fever and Neural Pathway from Liver

**By: Shozab Seemab Khan
(PhD Zoology Scholar)**

ABAIIDULLAH COLLEGE PAKPATTAN



What Is Fever?

- Fever is a regulated rise in body temperature above the normal range (typically $> 38^{\circ}\text{C}$ or 100.4°F), triggered by the hypothalamus in response to infection, inflammation, or injury.
- Fever is not a disease, but a defense mechanism to enhance immune response and inhibit pathogens.



What Is Fever?

-  How Fever Is Generated?
- **Overview of the Pathway**
- Fever is stimulated by a neuro-immune pathway involving signals from peripheral organs (like the liver) to the brain, especially the hypothalamus, which sets the body's "thermostat."

Step-by-Step Mechanism of Fever

- **1. Infection or Inflammation:** Bacteria, viruses, or damaged tissues release pathogen-associated molecular patterns (PAMPs) or damage-associated molecular patterns (DAMPs).
- **2. Cytokine Production (Especially in Liver):**
 - Immune cells (macrophages, Kupffer cells in the liver) produce pro-inflammatory cytokines, mainly:
 - Interleukin-1 (IL-1)
 - Interleukin-6 (IL-6)
 - Tumor Necrosis Factor-alpha (TNF- α)
 - These cytokines act as endogenous pyrogens.

Step-by-Step Mechanism of Fever

• 3. Liver as a Key Sensor and Signal Relay

- Liver detects circulating PAMPs/DAMPs via immune receptors (e.g., TLRs).
- Produces IL-6, which enters circulation or signals via sensory nerves.
- The vagus nerve carries signals from the liver to the brain.
-  **Neural pathway:**
- Liver → Vagus nerve → Brainstem → Hypothalamus

Step-by-Step Mechanism of Fever

- **4. Signal Reaches the Brain (Hypothalamus)**
- Cytokines or neural signals stimulate endothelial cells in the **Organum Vasculosum of the Lamina Terminalis (OVLT)**, a specialized part of the hypothalamus lacking a blood-brain barrier.
- These cells produce prostaglandin E_2 (PGE_2) via COX-2 enzyme.

Step-by-Step Mechanism of Fever

- **5. PGE₂ Raises Hypothalamic Set Point**

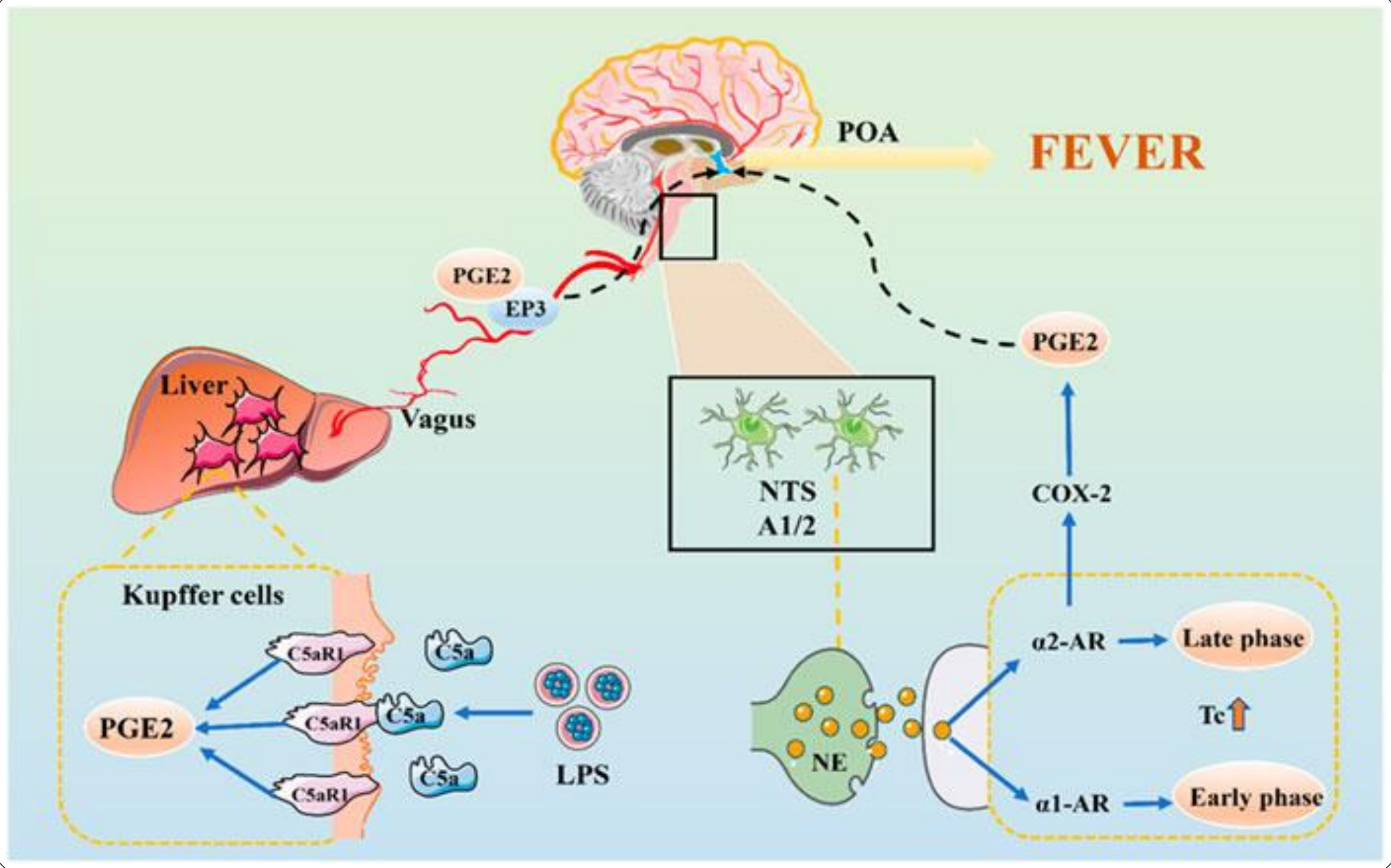
- PGE₂ binds to EP3 receptors in the preoptic area (POA) of the hypothalamus.
- This resets the body's thermostat to a higher temperature.

- **6. Physiological Changes to Raise Temperature**

- Vasoconstriction (less heat lost through skin)
- Shivering (generates heat)
- Behavioral responses: seeking warmth, wearing clothes

Summary Diagram of Pathway

- Infection/inflammation → PAMPs/DAMPs → Liver/Kupffer cells → IL-6, IL-1, TNF- α
- ↓
- Vagus nerve (afferent)
- ↓
- Brainstem → Hypothalamus (OVLT & POA)
- ↓
- COX-2 → PGE₂ → EP3 receptor
- ↓
- ↑ Hypothalamic set point → Fever response



Clinical Importance

- Fever is beneficial in moderation: enhances immunity, slows pathogen growth.
- Antipyretics (e.g., NSAIDs, paracetamol) work by blocking PGE₂ production.
- In liver failure, cytokine signaling may be impaired, altering fever response.
- Vagus nerve stimulation has been studied as a way to modulate fever and inflammation.

THANK YOU