Path 203 – Principles of Immunology
Lecture for undergraduate studies - Week 3

An acquired immune response is not the body's first choice. Therefore, if the pathogen can penetrate the natural and chemical barriers, the cells of the body also perform a non-specialized defense .

Cell defense in many ways , includes the followings:

i. **Fever (by secreted cytokine**
ii. **phagocytosis**
iii. **Inflammation**

So inflammation is the creation of an environment unsuitable for the invading pathogen to live and thrive .

*How does the body raise its temperature

*And how to calculate the temperature is a defensive way

Fever

Fever (also referred to as pyrexia) is defined as having a temperature above the normal range due to an increase in the body's temperature set point.

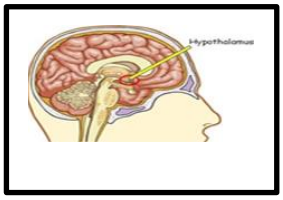
Fever is one of the most common medical signs. It is part of about 30% of healthcare visits by children and occurs in up to 75% of adults who are seriously sick. About 5% of people who go to an emergency room have a fever.

In adults, the normal range of oral temperatures in healthy individuals is 35.7–37.7 °C (96.3–99.9 °F) among men and 33.2–38.1 °C (91.8–100.6 °F) among women, while when taken rectally it is 36.7–37.5 °C (98.1–99.5 °F) among men and 36.8–37.1 °C (98.2–98.8 °F) among women, and for ear measurement it is 35.5–37.5 °C (95.9–99.5 °F) among men and 35.7–37.5 °C (96.3–99.5 °F) among women.

Normal body temperatures vary depending on many factors, including age, sex, time of day, ambient temperature, activity level, and more.

Hypothalamus

Temperature is regulated in the hypothalamus. the hypothalamus can be seen as working like a thermostat.



The increase in set point triggers increased muscle contractions and causes a feeling of cold. This results in greater heat production and efforts to conserve heat. When the set point temperature returns to normal, a person feels hot, becomes flushed, and may begin to sweat. Rarely a fever may trigger a febrile seizure, with this being more common in young children. Fevers do not typically go higher than 41 to 42 °C (105.8 to 107.6 °F).

A fever can be caused by many medical conditions ranging from non-serious to life-threatening. This includes viral, bacterial, and parasitic infections—such as influenza, the common cold, meningitis, urinary tract infections, appendicitis, COVID-19, and malaria.

Non-infectious causes include vasculitis, deep vein thrombosis, connective tissue disease, side effects of medication, and cancer

Factor that affect hypothyroidism and cause it to its lose ability to control body temperature are called pyrogens , and it may be its source internal(Endogenous).

or external (Exogenous)

Endogenous.

Major endogenous pyrogens are interleukin 1 (α and β). and interleukin 6 (IL-6).

Minor endogenous pyrogens include interleukin-8, tumor necrosis factor-β, macrophage inflammatory protein-α and macrophage inflammatory protein-β as well as interferon-α, interferon-β, and interferon-γ. Tumor necrosis factor-α (TNF)

These cytokine factors are released into general circulation, where they migrate to the brain's circumventricular organs where they are more easily absorbed than in areas protected by the blood–brain barrier. The cytokines then bind to endothelial receptors on vessel walls to receptors on microglial cells, resulting in activation of the arachidonic acid pathway.

These proteins produce a cyclooxygenase which induces the hypothalamic production of PGE2 which then stimulates the release of neurotransmitters such as cyclic adenosine monophosphate and increases body temperature. PGE2 release comes from the arachidonic acid pathway. This pathway (as it relates to fever), is mediated by the enzymes phospholipase A2 (PLA2), cyclooxygenase-2 (COX-2), and prostaglandin E2 synthase. These enzymes ultimately mediate the synthesis and release of PGE2.

Exogenous

Exogenous pyrogens are external to the body and are of microbial origin. In general, these pyrogens, including bacterial cell wall products, may act on Toll-like receptors in the hypothalamus and elevate the thermoregulatory setpoint.

An example of a class of exogenous pyrogens are bacterial lipopolysaccharides (LPS) present in the cell wall of gram-negative bacteria. According to one mechanism of pyrogen action, an immune system protein, lipopolysaccharide-binding protein (LBP), binds to LPS, and the LBP–LPS complex then binds to a CD14 receptor on a macrophage. The LBP-LPS binding to CD14 results in cellular synthesis and release of various endogenous cytokines, e.g., interleukin 1 (IL-1), interleukin 6 (IL-6), and tumor necrosis factor-alpha (TNFα). A further downstream event is activation of the arachidonic acid pathway.

The "pyrogenicity" of given pyrogens varies: in extreme cases, bacterial pyrogens can act as super antigens and cause rapid and dangerous fevers.