



# **Non Infectious Causes of Fever In Intensive Care Unit**

*Essay*

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in General Intensive Care

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## **Abstract**

**Background:** Fever is a common problem in the intensive care unit (ICU), which prompts important diagnostic and treatment decisions. Normal body temperature is approximately 37°C, although this varies with the time of day and the method of measurement used. The American College of Critical Care Medicine and the Infectious Diseases Society of America defined fever as a body temperature of 38.3°C or higher.

ARDS (both acute and late fibroproliferative phase), subarachnoid hemorrhage, transplant rejection, deep venous thrombosis, gout/pseudogout, hematoma, cirrhosis (without primary peritonitis), GI bleed, phlebitis/thrombophlebitis, IV contrast reaction, neoplastic fevers and decubitus ulcers.

**Aim of the Essay:** The aim of this essay is to discuss the non-infectious causes of fever in ICU patients as regard diagnosis and management and to differentiate it from other infectious causes.

**Methodology:** The regulation of body temperature is one of the myriad of interrelated functions essential to the maintenance of homeostasis that is controlled primarily through dedicated pathways in the brain.

**Conclusion:** Febrile patients should be monitored frequently with respect to vital signs, performance status, and the ability to achieve adequate oral intake. Temporarily holding administration of systemic chemotherapy should be considered during the management of the sepsis syndrome until the patient stabilizes.

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**Keywords:** Non-Infectious, Diagnosis and management, Intensive Care Unit

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

# قالوا

سببنا انك لا تعلم لنا  
إلا ما علمتنا إنك أنت  
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٣٢



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## **List of Abbreviations**

Abbreviation	Full Term
BAT	: Brown Adipose Tissue
CF	: Central Fever
CNS	: Central Nervous System
CO	: Carbon Monoxide
COX -2	: Cyclo Oxygenase 2
CVC	: Cutaneus Vaso Constriction
DMH	: Dorsal Medial Hypothalamus
DVT	: Deep Venous Thrombosis
ECG	: Electro Cardio Gram
FUO	: Fever of Unknown Origin
GABA	: Gamma Amino Butyric Acid
GAD	: Glutamic Acid Decarboxylase
ICV	: Intra Cerebro Ventricular
IFN	: Interferon
IL	: Interleukin
IML	: Inter Medio Lateral Nucleus
LPB	: Lateral Parabrachial Nucleus
LPBD	: Dorsal Subnucleus of the Lateral Para Brachial Nucleus
LPBeL	: External Lateral Subnucleus of the Lateral Parabrachial Neucleus

## *List of Abbreviations*

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LPO	: Lateral Pre Optic Nucleus
MnPO	: Median Pre Optic Nucleus
MPO	: Medial Pre Optic Nucleus
NICU	: Neurological Intensive Care Unit
NMDA	: N-Methyl D-Aspartate
NSAIDs	: Non Steroidal Anti Inflammatory Drugs
PE	: Pulmonary Embolism
PG	: Prostaglandins
POA	: PreOptic Area
rRPa	: Rostral Raphe Pallidus Nucleus
RYR-1	: Ryanodine Receptor Type 1
SAH	: Sub Arachnoid Haemorrhage
SNA	: Sympathetic Nerve Activity
SPNS	: Sympathetic Pre Ganglionic Neurons
TE	: Thrombo Embolism
TFTs	: Thyroid Function Tests
TNF	: Tumor Necrosis Factor
TRALI	: Transfusion Related Acute Lung Injury
TRP	: Transient Receptor Potential
UCP1	: Un Coupling Protein -1
VGLUT	: Vesicular Glutamate Transporter 3
VMM	: Ventro Medial Medulla

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## Introduction

Fever is a common problem in the intensive care unit (ICU), which prompts important diagnostic and treatment decisions. Normal body temperature is approximately 37°C, although this varies with the time of day and the method of measurement used. The American College of Critical Care Medicine and the Infectious Diseases Society of America defined fever as a body temperature of 38.3°C or higher (*O'Grady et al., 2008*).

Conventional means of measuring temperature in the ICU include intravascular, intravascular (ie, bladder), rectal, and oral. The gold standard is thermistor on a pulmonary artery catheter, although these are used infrequently and may give unreliable temperature readings if the catheter is used to rapidly administer volume regardless of which method is chosen, the same method and site of measurement should be used repeatedly to facilitate the trending of serial measurements (*Niven et al., 2015*).

Alternative methods, such as axillary, temporal artery, tympanic, and chemical dot monitors, should not be used because they are inaccurate during critical illness despite this inaccuracy, these methods are still in

widespread use in many ICUs around the world (*Nimah et al., 2006*).

Fever complicates up to 70% of all intensive care unit (ICU) admissions and is often due to an infection or another serious condition. In one observational study of 24,204 adult ICU admissions, fever  $\geq 39.5^{\circ}\text{C}$  was associated with an increase in mortality (20 versus 12%) (*Laupland et al., 2008*).

Fever has also been associated with an increased length of hospital stay, increased cost of care, and poorer outcomes in traumatic brain injury and critically ill patient. Fever may prompt unnecessary investigations and inappropriate antibiotic use (*Stocchetti et al., 2002*).

The importance of fever as a pathophysiological process is poorly understood. Although regarded as a sign of clinical deterioration, fever can be an appropriate adaptive response to infection. For example, one study showed that elevated peak temperatures  $39^{\circ}\text{C}$  to  $39.5^{\circ}\text{C}$  in ICU patients with infections were associated with decreased hospital mortality compared to patients with peak temperatures  $36.5$  to  $36.9^{\circ}\text{C}$ . However, in non-infectious cases of fever, mortality increased with rising temperature (*Young et al., 2012*).

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A large number of non infectious disorders result in tissue injury with inflammation and a febrile reaction such as alcohol/drug withdrawal, postoperative fever (48 h postoperative), post transfusion fever, drug fever, adrenal insufficiency, pancreatitis, acalculous cholecystitis, aspiration pneumonitis, ARDS (both acute and late fibroproliferative phase), subarachnoid hemorrhage, transplant rejection, deep venous thrombosis, gout/pseudogout, hematoma, cirrhosis (without primary peritonitis), GI bleed, phlebitis/thrombophlebitis, IV contrast reaction, neoplastic fevers and decubitus ulcers (*O'Grady et al., 2008*).

## **Aim of the Essay**

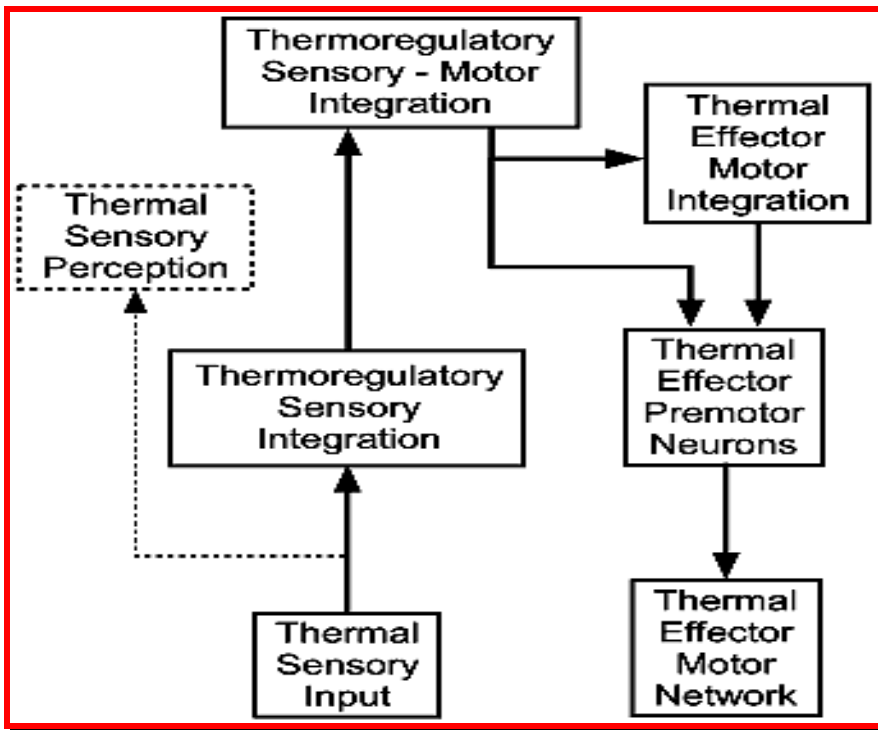
The aim of this essay is to discuss the non-infectious causes of fever in ICU patients as regard diagnosis and management and to differentiate it from other infectious causes.

## ***Chapter (I)***

# **Regulation of Body Temperature**

The regulation of body temperature is one of the myriad of interrelated functions essential to the maintenance of homeostasis that is controlled primarily through dedicated pathways in the brain (*Morrison and Nakamura, 2011*).

Hence, the brain is highly attentive to the potential for alterations in the temperature environment of its resident neurons and of the many tissues on which it depends for survival. The central neural pathways represented in the following figure (Fig. 1) (*Brown et al., 2012*).



**Fig. 1:** Block diagram of the functional components of a model for the central neural circuit providing cutaneous thermal afferent and thermally-sensitive neuronal control of thermo-regulatory effectors (*Brown et al., 2012*).

The core central thermoregulatory network comprises the fundamental pathways through which cutaneous and visceral cold and warm sensation and/or reductions or elevations in brain temperature elicit changes in thermoregulatory effector tissues to counter or protect against changes in the temperature of the brain and other critical organ tissues. The effector mechanisms for cold defense is illustrated in (Fig. 2) (*Morrison and Nakamura, 2011*).