Ain Shams University
Faculty of Medicine
Department of anesthesia, critical care and pain management



Fever in Intensive Care Unit patients

An essay submitted for the partial fulfillment of the master degree in intensive care

Presented by

Ahmed Tolba Mostafa
M.B.B.CH Alfayoum University

Supervised by

PROF. DR. Ahmed Ibrahim Ibrahim

Professor of Anesthesia ,Intensive care and pain management
Faculty of medicine
Ain-Shams University

DR. Amal Hamed Rabie

Lecturer of Anesthesia, Intensive care and pain management Faculty of medicine Ain-Shams University

DR. Mohammed Yousef Khashaba

Lecturer of Anesthesia, Intensive Care and pain management Faculty of Medicine Ain Shams University

> Faculty of Medicine Ain Shams University 2013

Acknowledgment

To **Allah**, goes all my deepest gratitude and thanks for achieving any work in my life.

I would like to express my profound gratitude & deepest appreciation to **Prof. Dr. Ahmed Ibrahim Ibrahim**, Professor of Anesthesiology and Intensive care, Faculty of Medicine, Ain Shams University, for his relentless support, constant advice, valuable instructions, continuous encouragement & for the time & effort he devoted throughout the entire course of the study.

I am deeply thankful to **Dr. Amal Hamed Rabie**, Lecturer of Anesthesiology and Intensive care, Ain Shams University, for her willing assistance, enlightening comments, splendid efforts as well as providing valuable criticism and direction along the entire course of the study.

And mygreatest thanks and appreciation to Dr. **Mohammed** Yousef Khashaba, Lecturer of Anesthesiology and Intensive care, Ain Shams University, for his precious efforts, help and kindness along the entire course of the study.

Last but not least, my deep appreciation is expressed to all **the staff of Anesthesiology and Intensive care Department**, Ain Shams University as well as to **all members of my family** for their cooperation and encouragement.

Ahmed Tolba,

Contents

		Pages
•	List of abbreviations	I
•	List of tables	. V
•	List of figures	VI
•	Introduction	1
•	Pathophysiology of fever	4
•	Causes of fever in intensive care unit	40
•	Management of fever in intensive care unit	64
•	Summary	110
•	References	113
•	Arabic summary	

List of Abbreviations

Abbreviation	Meaning
APR	Acute phase reaction.
ARDS	Acute Respiratory Distress Syndrome.
ATP	Adenosine Triphosphate.
ВВВ	Blood Brain Barrier.
°C	Celsius.
CAP	Community-acquired pneumonia.
CCU	Cardiac care unit.
CFU	Colony forming units.
СНСТ	Caffeine halothane contracture test .
СМ	Candida mannan.
CMV	Cytomegalo virus.
CNS	Central nervous system.
COX	Cyclooxygenase.
СРК	Creatinine Phosphokinase.
CRBSI	Catheter related blood stream infections.
CRP	C reactive protein.
CSF	Cerebrospinal fluid.
CT	Computerized tomography.
DNA	Deoxyribonucleic acid.
EIA	Enzyme immunoassay.

Abbreviation	Meaning
ELISA	Enzyme-linked immunosorbent assay.
EtCO2	End tidal carbon dioxide.
°F	Fahrenheit.
FC	Fragment, crystallizable.
GM	Galactomannan.
GIT	Gastrointestinal Tract.
HEV	High endothelial venules.
HS	Heat stroke.
HSF1	Heat shock factor-1.
HSPs	Heat shock proteins.
ICP	Intracranial pressure.
IL	Interleukin.
INF	Interferon.
Kcal.	Kilo calory.
LPS	Lipopolysaccharide.
MAO	Monoamine oxidase,
MDMA	3, 4-Methylendioxymeth- amphetamines.
МН	Malignant hyperthermia.
MRSA	Methicillin resistant staphylococcus aureus.
NK	Natural killer cell.
NO	Nitric Oxide.

Abbreviation	Meaning
NMS	Neuroleptic malignant syndrome.
NSAIDS	Non-steroidal anti-inflammatory drugs.
NST	Nucleus of tractus solitarius .
PAMPS	Pathogen associated molecular patterns
PCP	Pentachlorophenol.
PCT	Procalcitonin.
PFPF	Preformed pyrogenic factors .
PG	Prostaglandins.
РТН	Post traumatic hyperthermia.
SAH	Subarachnoid hemorrhage .
SIRS	Systemic inflammatory response syndrome.
SPP	Species.
SS	Serotonin Syndrome.
SSRIs	Selective serotonin re-uptake inhibitors.
STICU	Surgical and trauma intensive care unit.
TBI	Traumatic brain injury.
Тс	Core temperature.
Th	T helper cell.
TNF	Tumor necrosis factor.
TLR-4	Toll like receptors 4
TPN	Total parenteral nutrition.

Abbreviation	Meaning
TRP	Transient receptor potential.
Tset	Set point temperature.
VAP	Ventilator associated pneumonia.
WCC	White cell count.

List of tables

No	Title	page
Table	Major syndromes and causes of	57
(1)	hyperthermia syndromes.	
Table	Medications commonly implicated in	58
(2)	serotonin syndrome.	
Table	Measurement of fever.	٦6
(3)		
Table	Factors that affect the accuracy and	٦8
(٤)	precision of various temperature	
	methods.	
Table	Management of Infectious Causes of	٧9
(5)	Fever in ICU.	
Table	Currently available methods and devices	۸5-90
(6)	for inducing and maintaining	
	hypothermia.	
Table	Catheter realated infections.	105
(7)		
Table	Management approach for most common	1.6
(8)	CR-BSI(Catheter related blood stream	
(-)	infection).	

List of figures

No	Title	page
Figure	Schematic representation of proposed	10
(1)	neuroimmune interactions that result in fever.	
Figure	Pathways for fever in bacterial infections.	11
(2)		
Figure	proposed methods of activation of	١4
(3)	hypothalamus.	
Figure	Proposed mechanism for protective and	۲4
(4)	detrimental effects of fever in sepsis.	
Figure	Simplified Pathophysiology of Neuroleptic	31
(5)	Malignant Syndrome, Including Elements of	
	Sympathoadrenal Dysregulation.	
Figure	Possible Pathophysiological Mechanisms of	٣6
(6)	Heat Stroke.	
Figure	The sequence of events in the progression of	٣7
(7)	heat stress to heat stroke.	
Figure	Mechanism of rhinosinusitis in the ICU	٤5
(8)	patients.	
Figure	Approach of management the febrile critically	72
(9)	ill patient.	

Introduction

Fever is common in intensive care unit (ICU). Its incidence ranges from 28 – 70 % of patients in general ICU and from 23 – 47 % in neurosurgical and neurological ICU (**Kiekkas et al., 2008**). In many ICUs, patients with temperature of 38.3 °C or more are considered to be febrile and special attention is warranted if infection is present (**O'grady et al., 1998**).

The definition of fever is arbitrary and depends on the purpose for which it is defined. Some literature defines fever as a core temperature of 38.0°C, whereas other sources define fever as two consecutive elevations of 38.3°C. In patients who are neutropenic, fever has been defined as a single oral temperature of 38.3°C in the absence of an obvious environmental cause, or a temperature elevation of 38.0°C for 1 hr. A variety of definitions of fever are acceptable, depending on how sensitive an indicator of thermal abnormality an ICU practitioner wants to utilize. Because fever can have many infectious and non infectious etiologies, a new fever in a patient in the ICU should trigger a careful clinical assessment rather than automatic orders for laboratory and radiologic tests. A cost conscious approach for obtaining cultures and imaging studies should be undertaken if indicated after a clinical evaluation (O'grady et al., 2008).

Evaluating a new fever in a patient in the ICU should begin with thorough history and physical examination. The main objective of management of a febrile patient is to identify the cause and eliminate it (**Tabah et al., 2010**). Fever is a common response to sepsis in critically ill patients. It occurs when either exogenous or endogenous pyrogen affect prostaglandin E2 synthesis (**Ryan and Levy, 2003**).

In about half the ICU patients, fever is secondary to a developing infection, in which case, bacteriologic samples are obtained and empiric antimicrobial therapy is initiated. The antimicrobial treatment must be continuously assessed even when treatment appears successful. Medications should be reevaluated when the laboratory results become available (**Tabah et al., 2010**). Efforts must be made to identify the source of infection and the causative organism, which may be a resistant hospital pathogen Fever in the critically ill patient, is a marker of an underlying problem which needs to be unearthed and suitably dealt with, rather than reacting to an elevated body temperature in a knee jerk fashion (**Kothari and karnad, 2005**).

An elevated body temperature may, however, be associated with a number of deleterious effects, most notably an increase in cardiac output, oxygen consumption, carbon dioxide production, and increase in BMR(basal metabolic rate). oxygen consumption

increases by approximately 10% per degree Celsius. These changes may be poorly tolerated in patients with limited cardiorespiratory reserve. In patients who have suffered a cerebrovascular accident or traumatic head injury, moderate elevations of brain temperature may markedly worsen the resulting injury. Maternal fever has been suggested to be a cause of fetal malformations or spontaneous abortion (**Kothari and karnad, 2005**).

Although nurses employ various techniques in attempting to cool critically ill patients, no guidelines have been established for the pharmacologic and physical treatment of fever. Although two newer physical antipyretic methods appear to be more effective at lowering temperature than conventional methods, they have significant drawbacks: one is highly invasive (endovascular cooling) and the other is associated with shivering (water circulating pads) (**Kiekkas et al., 2008**).

Temperature is the thermal state of an object (**Rajan and Rao, 2008**). Normal body temperature is generally considered to be 37.0°C (98.6°F) with a circadian variation of 0.5°C to 1.0°C (**Marik, 2000**).

The definition of fever is arbitrary and depends on the purpose for which it is defined. The Society of Critical Care Medicine practice parameters define fever in the ICU as a temperature >38.3°C (≥ 101 °F). Unless the patient has other features of an infectious process, only a temperature >38.3°C (≥ 101 °F) warrants further investigation (Marik, 2000).

Body Temperature is controlled by balancing heat production against heat loss. When the rate of heat production is greater than the rate at which heat is being lost, heat builds up in the body & the body temperature rises. Conversely, when heat loss is greater, both body heat and body temperature decrease(Marieb, 2009).

Heat loss mechanisms:

Heat is lost from the skin to the surroundings by radiation (60%), conduction (15%) & evaporation (22%). (**Guyton, 2006**).

Radiation is the transfer of heat by infrared electromagnetic radiation from one object to another at a different temperature with which it is not in contact. Because of radiation, an individual

can feel chilly in a room with cold walls even though the room is relatively warm (Barrett et al., 2010).

Conduction is heat exchange between objects or substances at different temperatures that are in contact with one another. The rate at which heat is transferred from the deep tissues to the skin is called the tissue conductance. Conduction is aided by convection (Barrett et al., 2010).

the transfer of heat resulting **Convection:** is from the movement of a fluid, either liquid or gas. In the fluid is usually air or water physiology, in the environment or blood in case of heat transfer in the body. Although conduction plays a role in this process, convection so dominates the overall heat transfer as that we refer to the heat transfer as if it is entirely convection. Therefore, the conduction term is restricted to heat flow between the body and other solid objects and it usually represents only a small part of the total heat exchange with the environment (Marieb, 2009).

Vaporization of water on the skin and mucous membranes of the mouth and respiratory passages. Vaporization of 1 g of water removes about 0.6 kcal of heat. A certain amount of water is vaporized at all times. This insensible water loss amounts to 50 ml/ h in humans. When sweat secretion is increased, the degree to