# ICU MANAGEMENT

VOLUME 8 - ISSUE 3 - AUTUMN 2008

THE OFFICIAL MANAGEMENT AND PRACTICE JOURNAL


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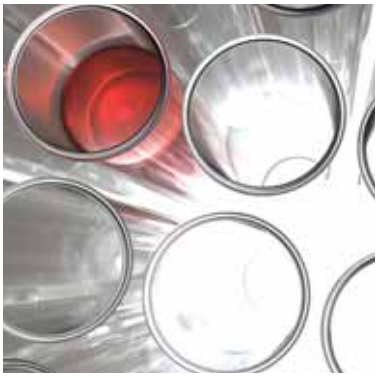
# EDITORIAL

Jean-Louis Vincent

**Editor-in-Chief**
ICU Management

**Head Department of Intensive Care**
Erasme Hospital
Free University of Brussels
Brussels, Belgium
jlvincent@ulb.ac.be



In critical care, there is no single answer, no magic solution - pharmaceutical or diagnostic that can cure all patients or improve their conditions simultaneously. In **ICU Management** we are always, however, in search of new diagnostic tools and medications, which we can add to our arsenal of weapons in fighting the deadliest of conditions that our patients face. While an ideal biomarker has not been identified, in recent years, several biomarkers have been highlighted in studies and research as possible tools in the early detection and treatment of certain infections.

In this issue of **ICU Management**, Dr. Povoa argues that biomarkers can provide additional information to the clinical evaluation in the diagnosis of infection, risk stratification, as well as in assessment of the response to antibiotic therapy. He looks at two such noted biomarkers: C-reactive protein (CRP) and procalcitonin (PCT), in addition to the newly proposed soluble triggering receptor expressed on myeloid cells-1 (sTREM–1) and evaluates their possible roles in the diagnosis of infection. Drs. Coelho and Pereira from Portugal focus solely on the use of serum biomarkers in the evaluation of infection response to antibiotics, while Dominique Vandijck from Ghent University Hospital examines the cost effectiveness of utilising biomarkers in the diagnosis of septic patients.

As the general population ages, so too does the number of elderly patients who come into our direct care in the ICU. Management of these patients - with their unique needs and treatment issues is a matter that requires renewed attention and increased vigilance of the part of ICU teams as a whole. Our special focus on care of the elderly begins with a thought-provoking article by Dr. Barraco from Pennsylvania, USA on how to reduce perioperative risk in your ICU; and will culminate in an issue of **ICU Management** next year on this timely and important issue for ICU managers and professionals.

**ICU Management** Editorial Board Member, Dr. Flaatten lends his time and expertise to outline the state of education and training in intensive care in Europe, a topic of much current study and discussion in the field.

In our continuing Hypothermia Series Dr. Polderman discusses fever control in critically ill patients, and in the Management segment of this issue, Rebecca Anas, Dr. Brunet and colleagues from Toronto, Canada return to **ICU Management** to introduce a framework to implement efficient, evidence based organisation of care in our units.

This time our Country Focus lands in Israel for a brief yet interesting visit: Dr. Gurman discusses the similarities and differences in the closely intertwined fields of anaesthesiology and intensive care in Israel, and in general. Freda DeKeyser Ganz outlines ongoing changes in intensive care nursing education in Israel, and Rabia Khalaila and team from Hadassah-Ein Kerem Medical Center in Jerusalem highlight the importance of physical assessments done by nurses in the ICU.

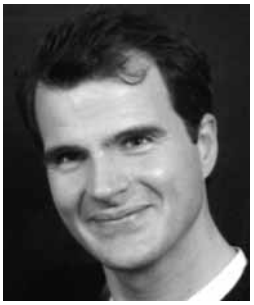
As we strive to provide the most efficient, accurate and favorable treatment for our patients-as critical care professionals, we look continuously toward science to provide more techniques to us in early diagnosis and treatments. A definitive, specific biomarker for sepsis is yet to be found, but as the authors in this issue concur, there are many beneficial uses for those markers that are readily accessible.

An added note - in this issue, we have elected to include references listed by contributing authors. We hope that this and our continuing evolution of format and style changes will continue to increase the interest and value **ICU Management**. Your comments and requests are always welcome. Please forward any correspondence to Managing Editor Sherry Scharff at **editorial@icu-management.org**

Jean-Louis Vincent

HYPOTHERMIA SERIES

# FEVER CONTROL IN CRITICALLY ILL PATIENTS



Kees H. Polderman, MD, PhD
**Associate Professor of Intensive Care Medicine**
Dept. of Intensive Care
Utrecht University Medical Center
Utrecht, The Netherlands

k.polderman@tip.nl
k.polderman@umcutrecht.nl

**Regional temperature differences exist between various parts of the body under physiological conditions in healthy individuals. Traditionally, a temperature gradient between the "core comparment" and the "peripheral compartment" has been recognised. The core compartment basically comprises the organs and rump of the body, while the periphery consists of the arms and legs. Temperature differences between core and periphery may range from 2 °C to 10 °C, depending on the temperature of the environment and other circumstances.**

It is less well known that small temperature gradients can also exist within the core compartment. Under normal circumstances (absent the presence of a local infection), the organ/area with the highest temperature within the core compartment is the brain.

In healthy individuals, brain temperature is only marginally higher than the measured core temperature; this difference typically ranges from 0.1-0.3°C. In addition, there are small temperature gradients between different areas of the brain. These regional differences are related to activity (higher temperatures in more active brain tissue), blood flow (lower temperatures in areas with high flow due to increased capacity to dissipate and remove heat), and (to a lesser degree) to the distance from the skull (the latter being particularly important in newborns and very young children).

The differences in temperature between the brain and measured core temperature can increase significantly under pathological conditions, such as exist following various types of brain injury. Numerous studies have demonstrated that brain temperature in patients with traumatic brain injury, stroke, subarachnoid haemorrhage, encephalitis and other types of neurological injury exceeds measured core temperature by between 0.2°C and 4°C compared to the "gold standard", i.e. the blood temperature measured by pulmonary artery catheter, or compared to core temperatures measured at the oesophagus, bladder or rectum. Again, there are temperature differences between different areas of the brain; however, in contrast to the physiological situation these differences can be substantial, up to 2°C, with the highest temperatures found in injured areas of the brain. Many authors have described this phenomenon, and it is a frequent occurrence although the extent may vary considerably.

The mechanism underlying this phenomenon is the generation of excess heat by the ongoing pathophysiological processes in injured areas of the brain. It is well recognised that a period of ischaemia or trauma can trigger a cascade of numerous destructive mechanisms. Some of these produce heat, in particular the activation of neuroinflammatory processes, the increase in blood brain barrier permeability, and a phenomenon known as "exitotoxicity", a self-destructive "hyperactivity" of injured cells caused by a combination of cell membrane leakage, mitochondrial dysfunction, and excessive influx of calcium (Ca2+) into the cell, leading to intracellular calcium overload with excessive enzyme activation, continuous depolarisation and a permanent state of hyperexcitability. In addition, local or general oedema formation will complicate the removal of heat through lymph drainage and venous return, further adding to overheating of injured areas in a phenomenon known as "cerebral thermo pooling".

The differences between measured core and brain temperature can increase even further when a patient develops systemic fever, a problem that is frequently observed in patients with various types of neurological injury and which is associated with adverse outcome.

The clinical significance of these phenomena is that increasing evidence exists showing that high temperatures can be harmful, especially to injured (brain) cells. Numerous animal studies have demonstrated that (external) induction of hyperthermia significantly increases the risk and extent of neurological injury. Hyperthermia increases the risk that ischaemic areas will become necrotic or apoptotic; it can be detrimental even when it is of short duration, even when it is mild, and even when it occurs long after the initial injury. These effects become more pronounced if hyperthermia coincides with an episode of ischaemia, suggesting that ischaemic brain cells become even more susceptible to the harmful effects of fever.

Numerous clinical studies have confirmed that fever is indeed an independent predictor of adverse neurological outcome and increased mortality in various neurologic emergencies, including ischaemic stroke, sub-

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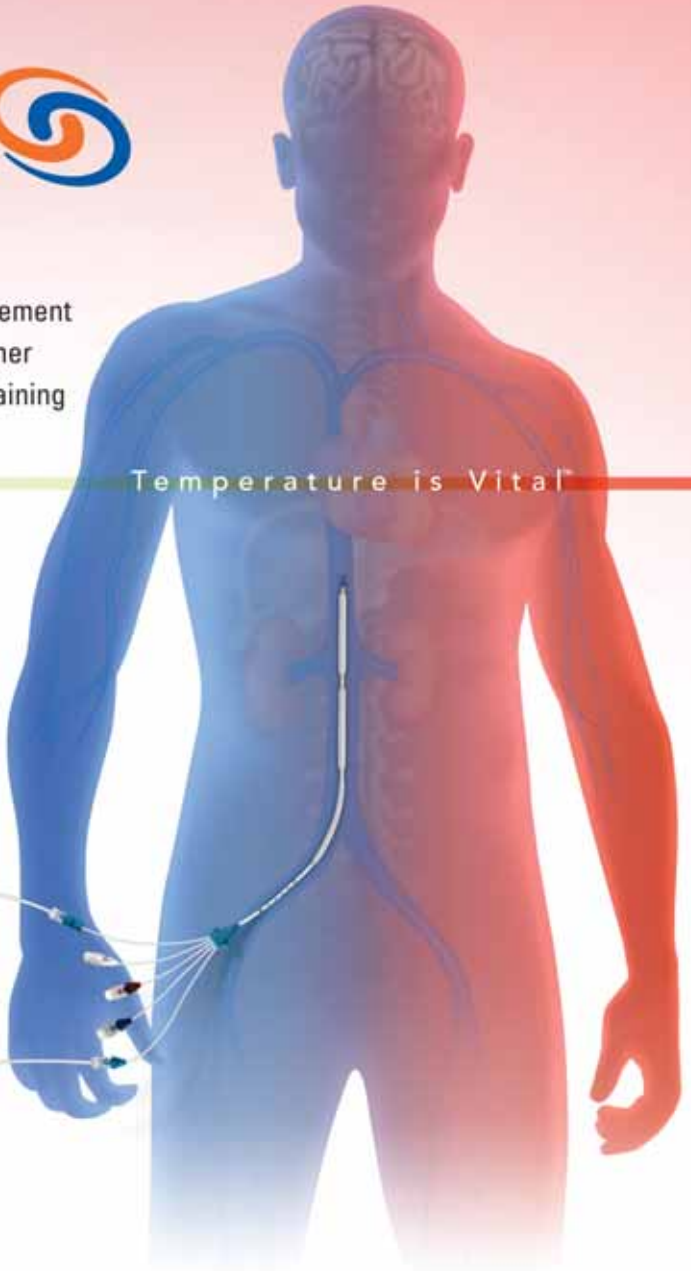


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arachnoid haemorrhage, intracranial haemorrhage, traumatic brain injury and post-anoxic injury. Azzimondi and co-workers performed a prospective observational study in stroke patients and observed that developing fever was associated with a 3.4-fold increase in the risk for adverse outcome, with a 95% CI of 1.2 to 9.5.[*] Castillo and associates reported that fever occurring within 24 hours after the onset of ischaemic stroke was independently related to larger infarct volumes (OR 3.23, 95% CI 1.63 to 6.43) and higher neurological deficits (OR 3.06, 95% CI 1.70 to 5.53) at 3 months. Kammersgaard et al. reported that each 1°C increase of admission body temperature independently predicted a 30% relative increase in long term mortality risk, with a 95% CI of 4% to 57%. Zeiner et al. observed that fever was associated with a 2.3-fold increase in the risk of adverse outcome in patients following cardiac arrest, with a p-value of 0.008.

Although these observations do not conclusively establish that the relationship between fever and increased neurological outcome is causal, i.e., that fever itself increases neurological injury rather than just being a marker, the temporal relationship, the fact that it persists after multivariate analysis, coupled with the results from animal experiments and the physiological data outlined above provide a strong and convincing framework for the existence of this relationship. This view is strengthened by observations from other animal studies showing that induction of mild hypothermia can prevent fever-related neurological injury, and can improve tissue tolerance for ischaemia.

All this suggests that lowering fever burden and lowering body temperature in febrile patients with neurological injuries could significantly improve outcome. Unfortunately, the use of anti-pyretic drugs is not very effective in this category of patients; various studies have shown that core temperatures decrease by (only) 0.1-0.7°C when adult patients with neurological injuries are treated with acetaminophen, aspirin or other anti-pyretic drugs. Therefore, mechanical cooling (with surface cooling devices or intravascular catheters) will usually be required to effectively control fever in these patients.

If this strategy could indeed prevent or reduce (additional) neurological injuries these interventions would obviously be tremendously cost-effective. Translating the observations and insights outlined above into feasible, practical and cost-effective protocols presents a worthy challenge to physicians caring for critically ill ICU patients. ■

**"Numerous clinical studies have confirmed that fever is indeed an independent predictor of adverse neurological outcome and increased mortality in various neurological emergencies."**

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[*] The *odds ratio* (OR) is a way of determining and comparing the probability of a certain event in two groups. For example: a survey taken among a sample of 100 hospital managers shows that 90 of them read ICU Management. A survey among 100 ICU physicians shows that in this group only 20 read this journal. The odds of a hospital manager reading ICU Management are 9 to 1; the odds of an ICU physician reading the journal are 1 to 4, or 0.25 to 1. The odds ratio is thus 9 divided by 0.25, or 36, showing that hospital managers are much more likely to read ICU Management than ICU physicians.
The *confidence interval* (CI) is a statistical range with a specified probability that a given parameter lies within the range. Confidence intervals are used to indicate the reliability of an estimate or measurement, i.e. to assess the likelihood that the difference is genuine with a likelihood of 95% (the 95% CI) or 99% (the 99% CI).

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**PROGRAM OVERVIEW**
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