The Brain Is Not Dead When the Cortex Is Dead

To the Editor:

In a recent issue of Critical Care Medicine, with interest we read the article by Dhanani et al (1), concerning vital signs after circulatory arrest following withdrawal of life-sustaining therapy. The article has timely given the persistent controversy regarding criteria of death in circulatory death organ donors. How many minutes after circulatory arrest can we consider the patient dead respecting the dead donor rule?

As brain activity is a crucial determinant in the concept and determination of death. The authors state that, based on their limited observation that neurologic function could permanently cease prior to the 5-minute wait period, required for circulatory death organ donation. They came to this conclusion on electroencephalographic (EEG) recordings in four patients, among which in one patient delta-waveform activity persisted following cessation of the electrocardiogram and arterial pressure. We think that this conclusion is to easily reached.

With surface EEG recording, only the outer layer of the cerebral cortex can be reached. It is incorrect to state that based on this clinical observation, neurologic function had permanently ceased. It is recently recognized that the cerebral cortex and hypothalamus share massive bidirectional connections. Pessoa (2) concluded that “the hypothalamus is involved in a host of basis control functions. It is part of an extensive bidirectional system with cortex and many subcortical structures, in a manner that allows for extensive integration of cognitive and emotional information.” As the deeper structures of the brain are more resistant to hypoxia than the cortex (3), we should be very careful stating that “neurologic function permanently has ceased” prior to the 5-minute waiting time after only recoding surface cortical activity.

Dr. Kompanje has disclosed employment, lectures, and royalties. Dr. Bakker has disclosed that he does not have any potential conflicts of interest.

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REFERENCES


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The authors reply:

We thank Kompanje and Bakker (1) for their interest and perceptive comment on our article (2).

The response raises the point that cessation of cerebral cortical activity, as reflected by scalp electroencephalogram (EEG), is not equivalent to “whole-brain death.” We agree with this comment and their statement that the brain stem is more resistant than the cortex to lack of blood flow. However, our discussion reflected that once cortical function is lost during the withdrawal process, it is not regained. We used the EEG as a tool to look for reversibility of recovery of activity of this accessible and assessable part of the brain. Reversibility is a key issue in the context of pronouncement of death using circulatory criteria. We were not looking to satisfy the criteria for brain death. However, it follows that if cortical function were irreversibly lost, once brainstem neurons are affected in due proportion, as they ultimately would be, their function would also not recover.

We would like to reemphasize that the primary objective of our study was to assess feasibility of collecting vital sign data during the dying process. The data that were subsequently reported regarding the pattern of loss of electrocardiogram activity, arterial blood pressure, and EEG activity should be viewed with extreme caution, and no firm conclusions should be made. It is clear that future studies promoting safe practice for donation after circulatory death will need to identify not only cessation of circulation but more importantly cessation of neurologic activity and function (3). We are excited to be able to progress with a larger study to observe and record physiologic data after withdrawal of life-sustaining therapies, which will help us uncover the natural history of cessation of both circulation and neurologic activity and function in dying patients. This information will help inform future policy and practice.

Design and implementation of the study and manuscript development were coordinated at the Children’s Hospital of Eastern Ontario.

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Dr. Dhanani consulted for and is chief medical officer of Trillium Gift of Life Network, Ontario. Ms. Hornby consulted for Canadian Blood Services and received grant support from the Canadian National Transplant Research Program. Dr. Shemie consulted for and is medical lead of Canadian Blood Services. Dr. Young consulted for GE Healthcare (EEG monitoring in intensive care patients).
Improvement in tissue perfusion and cellular metabolism can influence both these factors, resulting in decreased lactate levels, as shown in Figure 1. This is in contrast with the resolution of hyperlactatemia following grand mal seizures (8), in which overproduction stops abruptly and the decrease in blood lactate levels is just the result of clearance. The study of lactate clearance per se would require a lactate infusion, as performed by Levraut et al (9), making this a much more complex measurement. Monitoring lactate levels over time is a reflection of both production and clearance and provides valuable information regarding a patient’s response to therapy.

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REFERENCES

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Figure 1. The concept of the time course of blood lactate concentrations during the resolution of shock: production (line A) progressively decreases as clearance (line B) increases. Please note that the lines are not driven by data; the decline in lactate levels is not necessarily linear.

Serial Blood Lactate Levels Reflect Both Lactate Production and Clearance

To the Editor:

In a recent issue of Critical Care Medicine, Zhang and Xu (1) provided an interesting review on the value of using repeated lactate levels to guide therapy. More than 30 years ago, my colleagues and I were the first to propose that the change in blood lactate levels should be monitored during the treatment of shock. In that early study in a small number of patients, we reported that those who responded well to rapid fluid administration showed a more than 5% decrease in lactate concentrations over the first hour of treatment, compared with those who did not respond in whom blood lactate levels were unchanged (2). We subsequently showed in several studies that blood lactate levels decrease more quickly and more consistently in patients with better outcomes (3, 4). We suggested that monitoring blood lactate levels over time could help to insure that treatment was effective. If blood lactate levels do not decrease, we should be encouraged to review and perhaps change our therapeutic strategy.

In their review, Zhang and Xu (1) stress the prognostic value of decreasing blood lactate levels. However, like others (5, 6) and even Puskarich and Jones (7) in their accompanying editorial, they incorrectly “reduce” the concept to an issue of “lactate clearance.” Levels of blood lactate, as indeed blood levels of any other substance, represent a balance between both the production and the elimination of lactate. In shock, increased production and decreased elimination are present.

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REFERENCES

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