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#### In Reply:

We thank Albin for his interest in and for important comments regarding our article.<sup>1</sup>

His first comment regarding the experimental design was to have another control group of animals that are anesthetized but not arrested. In our study, we used Japanese monkeys to avoid the effects of carotid rete by which many experimental animals can selectively decrease brain temperature with panting. Because we have to reduce the number of animals for compliance with the 3R principles, we examined the effect of pharyngeal cooling in one anesthetized animal. The results were shown in figure 5.

The next comment was related to the unit of cerebral blood flow (CBF) and the residual CBF during cardiac arrest. It has been reported that laser Doppler flowmetry does not measure absolute CBF; rather, it accurately measures relative changes in absolute CBF.<sup>2</sup> In our article, therefore, we presented CBF with percent changes of its preischemic value. At the end of cardiac arrest, all animals showed ventricular fibrillation, and CBF was decreased to  $7 \pm 4\%$  and  $5 \pm 3\%$  of the preischemia level in the treated and control groups, respectively. It is unlikely that the 2% difference in CBF indicated a significant difference in blood flow reduction during cardiac arrest. It is more likely that decrease in blood flow exceeded the level at which accurate measurement can be performed by Doppler flowmetry.

The comment about the flow rate of perfusate is an important issue. In our study, the flow rate of perfusate was 500 ml/min in both the monkey and patients regardless of body weight ( $8.2 \pm 2.1$  kg *vs.*  $47.3 \pm 12.4$  kg) and cuff volume (size 2, 40 ml *vs.* size 4, 115 ml). Because core brain temperature in the anesthetized monkey and tympanic temperatures in patients were similarly decreased by  $0.9^\circ\text{C}$  and  $0.6^\circ \pm 0.1^\circ\text{C}$ , respectively, during 30 min of pharyngeal cooling, we assumed that the flow rate of 500 ml/min exceeded the optimum flow rate for monkeys. However, we need to evaluate the optimum flow rate in each cuff size in the future.

We demonstrated that pharyngeal cooling can rapidly and selectively decrease brain temperature. However, because 20% of cardiac output circulates in the brain in normal conditions, it seems that a long duration of brain cooling eventually decreases whole body temperature. Therefore, we would like to use pharyngeal cooling during the acute phase of brain ischemia, especially during cardiac

arrest. After recovery of spontaneous circulation, pharyngeal cooling would be replaced by another cooling technique that decreases whole body temperature. For the induction of whole body cooling, intravenous infusion of cold saline is recommended.<sup>3</sup> For maintaining a stable temperature at  $32^\circ\text{--}34^\circ\text{C}$  for 24 h, an endovascular cooling system or a gel-coated pad cooling system has been reported to be reliable.<sup>4</sup>

Brown *et al.*<sup>5</sup> reported the effects of nasal cooling in an animal study in 1964. To date, several researchers have successfully shown decrease in brain temperature with a nasal or nasopharyngeal cooling technique, with different approaches.<sup>6</sup> To the best of my knowledge, various effects of nasal or nasopharyngeal cooling on tympanic temperature in humans were measured in seven studies, including our study.<sup>7–12</sup> We cited two of these reports. Our study is the first study in which a pharyngeal cooling cuff was used in humans. Because we should avoid subcutaneous emphysema or edema due to direct contact of cold air or fluid in the nasal and pharyngeal regions, we made a pharyngeal cooling cuff that is similar in shape to the supraglottic airway device. The shape was carefully decided by three-dimensional contrast-enhanced computed tomography images and cadaver dissections to fit the pharynx and carotid arteries. The channel in the cooling cuff was designed by thermal fluid analysis to increase the efficacy of cooling.

Albin suggested increasing the bibliographic review in the article. We agree with his suggestion because we can realize what we need to do by learning from previous works. However, our article focused on clinical application of the pharyngeal cooling technique. Therefore, we cited articles in which results of clinical trials were presented.

**Yoshimasa Takeda, M.D., Ph.D.,\* Hiroshi Hashimoto, B.Eng., Koji Fumoto, Ph.D., Tetsuya Danura, M.D., Hiromichi Naito, M.D., Naoki Morimoto, M.D., Ph.D., Hiroshi Katayama, M.D., Ph.D., Soichiro Fushimi, M.D., Ph.D., Akihiro Matsukawa, M.D., Ph.D., Aiji Ohtsuka, M.D., Ph.D., Kiyoshi Morita, M.D., Ph.D.** \*Okayama University Medical School, Okayama, Japan.

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## Regarding William T.G. Morton

### To the Editor:

I read with interest the July 2012 psychological analysis of William T.G. Morton,<sup>1</sup> developed nearly 150 yr after his death. I was pleased the authors gave readers wiggle room relative to their opinions about the article *via* phrases such as: “Retrospective psychiatric evaluations are inherently speculative and not diagnostic...”, “...a historical review of a person’s life cannot make a reliable diagnosis...”, and “...there is good reason to wonder whether a retrospective psychological analysis is valid.”

None of us were alive when Morton was, and we must depend on the documents generated by others in developing opinions about the man. The authors have referenced several recognized histories, but the list is far from all-inclusive of what has been written about Morton, and others, during the nascent days of anesthesia.

Nearly all references by the authors regarding Morton’s alleged lapses came from the articles by Charles T. Jackson. Jackson, Morton’s Letheon co-patent holder,<sup>2</sup> was Morton’s main antagonist during controversial discussions about who

deserved primacy for the discovery (to first observe and make known) of safe, reproducible, anesthesia. From my reading, it seems that Jackson was maniacally driven in his efforts to be recognized for any significant discovery and was willing to devote considerable time, energy, and resources to accomplish that goal, most often by usurping the efforts of others. Jackson tried to lay claim to era breakthroughs such as Beaumont’s gastric studies (1838), Morse’s telegraph (1844), Schonbein’s guncotton (1845), and finally, Morton’s ether (1846). Jackson was not a disinterested or objective source about Morton.

Elizabeth Whitman Morton was also not disinterested but was fully supportive of Morton as a husband and doctor until the end of her life. In 1896, Mrs. Morton shared many memories, including how seriously Morton took his medical studies, rising daily at 4:00 a.m. to study the boney anatomy of the skeleton in their bedroom before going to his dental practice. Later, for months, every spare hour was spent in experiment (with ether). Morton then observed humans, including himself, under ether’s influence nonsurgically before finally beginning to use it in his dental practice. Mrs. Morton described how she tried to dissuade Morton through the night October 15, 1846, from keeping his appointment at the Ether Dome the next day. In her mind, the potential benefits of the planned experiment were far outweighed by the risks of failure, perhaps even the patient’s death, potentially followed by a charge of manslaughter. Finally, Mrs. Morton mentions her husband’s volunteerism providing anesthesia in the (Civil) War.<sup>3</sup> Mrs. Morton does not seem to feel Dr. Morton was an antisocial narcissist.

Regarding the authors’ statement that Morton was derelict in not further developing a specialty in anesthesiology, there were not specialties in anything at that time, although the surgeons and nonsurgeons were fairly distinct. The fact that it took nearly 100 yr for the specialty to be established in medicine is not due to Morton’s lack of interest. After Ether Day, Morton continued to devote his clinical efforts to anesthesia-related activities, while Horace Wells, later acknowledged by the American Dental Association<sup>4</sup> and American Medical Association<sup>5</sup> as the discoverer of anesthesia, began other projects unrelated to anesthesia or dentistry after his December 1844 demonstration at the Ether Dome.

If indeed Morton was as narcissistic as the authors suggest, their statements such as: “...full of confidence and probably had an inflated self-image...”, “...expected the accolades to come ...quickly and easily...”, and “...there was little thought to providing pain relief during surgery as part of Morton’s own personal agenda...” might be valid. At this time, I remain unconvinced.

**Daniel L. Orr II, D.D.S., M.S.(Anesth.), Ph.D., J.D., M.D.**, University of Nevada, Las Vegas School of Dental Medicine, Las Vegas, Nevada. daniel.orr@unlv.edu