our findings concluded that the decrease in NF-κB activation in the hepatocytes in LPS OJ14 mice caused massive hepatocyte apoptosis, leading to secondary necrosis.  

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References  


Response to “Pathophysiology and treatment of the systemic inflammatory response syndrome from the perspective of evolutionary medicine”  

To the Editors:  
I would like to take this opportunity to respond to the comments by Dr. Fujita concerning my recent evidence-based surgical hypothesis article, “Reciprocal gut-brain evolutionary symbiosis provokes and amplifies the post-injury systemic inflammatory response syndrome,” which appeared in the November 2009 issue of Surgery.  

First, I would like to thank Dr. Fujita for his thoughtful comments. However, there is a need to correct a number of inaccuracies contained in his letter as well as take issue with his conclusion. Dr. Fujita states, incorrectly, that there is little evidence for cross-talk between the gut and the brain in humans. Although the number of studies in humans examining such cross-talk is small, nevertheless there are a wide and ever increasing number of studies in animals that are elucidating the extraordinary amount of cross-talk that occurs between the gut and brain, with the vagus nerve being the chief conduit of such informational exchange.  

That there are fewer studies in humans is fully understandable from the vantage point that the demonstration of cross-talk involves experimental manipulation that can only be applied in animal systems. There can be little reason to doubt that the demonstration of cross-talk in animal systems does not extend to humans. Furthermore, Dr. Fujita asserts in his letter that I refer to evolutionary principles applying to information flowing from a “leaky” gut. In fact, nowhere in my hypothesis article do I make this assertion, let alone even use or refer to the term “leaky gut.”  

More important, I must as well take exception to Dr. Fujita’s conclusion that “the appropriate treatment of [systemic inflammatory response syndrome] SIRS may not be deducible from evolutionary considerations.” The fundamental defining aspect of SIRS, that postinjury the body initiates a set of responses that seemingly run counter to not only the individual’s own recovery but also the clinician’s sustained efforts at palliative therapy, begs the question of “why” the body would generate and maintain such a response. It would seem a reasonable supposition that, because it is the body that initiates and maintains the inflammatory condition, the answer may lie in the evolutionary programing with which the body deals with injury. As such, the question of “why” becomes paramount and one for which an approach utilizing evolutionary medicine is ideally suited.  

Finally, the most salient reason why an evolutionary approach to the management of SIRS, as well as aiding in the design of new therapeutic modalities, should be considered is that the vast majority of current and experimental therapeutic approaches in the treatment of SIRS have not resulted in any major reduction in mortality and morbidity. Current and experimental treatments that are overwhelmingly based on a reductionist approach targeting specific points in the inflammatory response have not been able to circumvent the body’s overall drive to maintain the inflammatory response in the first place. Dr. Fujita’s rationale that “what is functional from an evolutionary perspective is not necessarily functional from the perspective of patients” may have some validity, but in the case of SIRS the continued high mortality and morbidity demand that new approaches be considered. Evolutionary medicine, which seeks to understand the mechanisms governing the body’s programming in response to injury, may provide the theoretical basis for understanding the shortcomings of current therapeutic modalities as well as the design of new ones in the treatment of SIRS.  

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3. None of the patients of Cothren et al3 had a septic abdomen, whereas in our study, all patients had severe sepsis.2

4. Cothren et al3 study is a case series, mainly demonstrating the technique. Our study is a randomized controlled trial, demonstrating that VAC with retention sutures is better than VAC alone.2

After considering these points, we easily could explain the differences concerning primary closure, average time to closure, and average number of re-explorations. The similarities of the 2 studies reside only in the technique of sequential fascial closure. The post-trauma (nonseptic) patient is easier to handle than the septic one.

The following list is in regard to the rest of the points concerning Dr Velmahos1:

1. The agreement rate of the relatives of the critically ill patients undergoing laparostomy to participate in the randomized clinical trial is indeed high for U.S. standards, which is a result of the etiology of laparostomy. The social background of a trauma patient requiring laparostomy (the most common reason for laparostomy in the United States) is different from that of a septic (nontrauma) abdomen (the most common reason for laparostomy in Europe). For example, it is certainly more complicated to find the relatives of a gunshot victim in an emergency situation than to discuss with an actively involved family background. The difference concerning the mentality of this background is well illustrated in the movie My Big Fat Greek Wedding (2002).

2. Concerning the low primary closure rate (40%) that we had in comparison with the rate reported in Dr Velmahos’s clinic (two-thirds of patients with open abdomen), we believe that the reason for this difference resides in the etiology of laparostomy, as mentioned previously. Our primary closure rate is consistent with prior publications (range, 30–67%).3

3. Delayed herniation is a phenomenon requiring at least 2 years of observation; we therefore expect to have more reliable results by the end of 2011. The results up to date, however, are encouraging.

4. Finally, no information was found concerning fascial dehiscence because we did not encounter this problem (neither did Cothren et al).

We were encouraged by Dr Velmahos’ comment, whose great experience and skeptical regard pointed out several interesting inquiries. We join him in his last of phrases and wish that our study would be a stimulus to other surgeons to use this technique and to decide for themselves on its purported benefits. Furthermore, we commit ourselves to continue to publish our experience with more patients and long-term results.

References