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CORR Insights

CORR Insights®: Do Inflammatory Markers Portend Heterotopic Ossification and Wound Failure in Combat Wounds?

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Where Are We Now?

Although modern military safety equipment appears to protect some soldiers from penetrating injury, it can also leave them subject to the massive blast injury trauma. The contemporary military surgeon is faced with the Herculean task of treating massive bone and soft tissue injury, while relying mostly on clinical assessment. The Regenerative Medicine Team from the Naval Medical Research Center is making progress in describing the massive, but poorly regulated immune response to blast injury. In previous work [1–3], the Regenerative Medicine Team identified numerous cytokines and chemokines produced in this response. Interestingly, some cytokines such as Il-6 are associated with acute inflammatory response, while others appear to be associated with osteogenesis and may contribute to the formation of heterotopic ossification (HO).

Where Do We Need To Go?

Forsberg and colleagues measured 24 cytokines and chemokines from serum and wound effluent in 200 wounded soldiers and correlated their expression with the development of HO and failure of delayed wound closure. The authors found that specific cytokines, among other factors, were associated with these complications. The associations with HO were stronger compared to wound failure, but it should be noted that the impressively low rate of wound failure probably contributed to the results. The disciplined and exacting care for severely injured soldiers at this institution was phenomenal. The low rate of wound infection reported by the authors is impressive given the severity of these wounds and the complexity of the transport of these wounded soldiers. Perhaps the authors should study other variables such as residual pain, weight loss or time to resumption of independent use of the limb rather than wound failure rate.

How Do We Get There?

Much work remains before these results produce clinical breakthroughs. I am

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sure the authors would describe this study as a pilot. The authors produced the data from samples taken at various times from injury. As a result, the chronology of the immune response from the moment of injury cannot be described. This information will be critical if the military surgeon plans for HO prophylaxis. Animal models are helpful when studying the role of specific cytokines and chemokines. Classically, knockout genetic models are extremely useful in clarifying the effect of specific agents. Alternatively, anticytokine antibodies have been used as in rheumatoid arthritis not only to clarify mechanisms of disease but as therapeutic agents as well. Since the use of animal models for blast injuries may lack relevance to the human host and may be difficult to perform for ethical reasons, perhaps anticytokine agents provide a more practical path. Finally, since the volume of clinical cases will hopefully decrease as foreign conflicts are resolved, the translation of this work to civilian injury may be necessary. In any event, it is important that the authors be assured that their important work will be supported in the future.

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