

WG 1 (Chemical, Biological, Radiological and Nuclear materials)

Neutrophil Extracellular Trap (NET) Degradation Attenuates Acute Lung Injury and Protects Mice from Ricin-Induced Acute Respiratory Distress Syndrome (ARDS)

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Ricin, a plant-toxin derived from the seeds of *Ricinus communis*, irreversibly inactivates ribosomes by site-specific depurination, thereby arresting cell protein synthesis. Pulmonary exposure to ricin represents a bona fide model for acute respiratory distress syndrome (ARDS) characterized by an intense pulmonary inflammation involving massive neutrophil recruitment accompanied by a severe disruption of the alveolar-capillary barrier leading to life-threatening pulmonary edema, compromised gas exchange and respiratory failure. We have previously shown that following pulmonary ricin intoxication there is a massive infiltration of neutrophils to the inflamed lung that damage the parenchyma by metalloproteinase dependent proteolysis of cell-cell junction proteins. Neutrophils are known to form neutrophil extracellular traps (NETs), as a part of innate mechanism for pathogen clearance. However, it is evident that NETs have detrimental impact in sterile inflammations, as in the case of ricin intoxication. In the current study we show that following pulmonary ricin intoxication, there is an increase in the levels of the nuclear enzyme protein-arginine deiminase 4 (PAD4) followed by histone citrullination, chromatin decondensation and DNA release from neutrophils, which are hallmarks of NETosis. In addition, we show that neutrophils efficiently produced NETs in the lungs of ricin exposed mice. Innovative treatment of ricin exposed mice with PEGylated long-acting recombinant DNase (PRX-119), targeted against NET-associated extracellular DNA, administered in combination with ricin specific antitoxin, dramatically decreased the levels of extracellular DNA, effectively mitigated lung damage and significantly reduced the disruption of the alveolar-capillary barrier. Moreover, this combined treatment facilitated attenuated reduction in body weight, accelerated recovery and conferred higher protection levels to mice in comparison to sole administration of antitoxin. This data highlights the potential clinical benefit of NET inhibition drugs in pulmonary ricinosis.

WG 2 (Preventive Medicine and Healthcare Policies)

General Introduction, Methods, Change in Perspective

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Military public health units play a crucial role in supporting forces, including cross-border operations, by implementing proactive, continuous, and innovative disease prevention measures. The Iron Swords War presented unique challenges that significantly affected epidemiological conditions on the battlefield. Prolonged deployments in enemy territory, contact with local populations in unsanitary and densely populated areas, poor living conditions in abandoned locations, and exposure to contaminated food and water heightened the risk of disease outbreaks.

To mitigate health risks and maintain operational readiness, military public health services adopted a holistic and adaptive approach, integrating preventive strategies, immediate interventions, and information dissemination. The implementation of high-standard operational procedures ensured the rapid prevention of infectious diseases and effective outbreak management. Key measures included vaccination operations, pest control, environmental sanitation, and stray animal management, alongside the distribution of protective resources.

To ensure operational readiness, military health services implemented evidence-based prevention strategies, including immediate intervention, information dissemination, and the allocation of tailored medical resources. An analysis of morbidity trends highlighted the importance of stringent operational protocols, enabling rapid disease prevention and effective outbreak management during prolonged combat.

A hygiene and sanitation approach were established to safeguard soldiers from infectious diseases and to enable effective combat execution. By reinforcing combat units with qualified personnel and cross-functional teams, the military public health system provided consistent medical support to frontline forces. This approach not only prevented illness but also allowed commanders to remain focused on their operational objectives.

The experience gained during the Iron Swords War contributed to the modernization of military health procedures, improving disease control strategies for future conflicts. The success of these interventions underscores the critical role of military public health services in sustaining combat readiness and protecting forces in prolonged and complex military operations.