Community-acquired pneumonia infections by Acinetobacter baumannii
How does alcohol impact the antimicrobial functions of macrophages?

Eliseo A Eugenin
Public Health Research Institute and Rutgers University Medical School; The State University of New Jersey; Newark, NJ USA

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In this issue of Virulence, Asplund et al.\(^1\) provides a proof of principle study indicating that physiological concentrations of alcohol impair macrophage antimicrobial functions against Acinetobacter baumannii (Ab). Thus, this communication delivers seminal evidence that alcohol and macrophages play a key role in the pathogenesis of Ab.

Ab is a wide spectrum of intrinsic and acquired multidrug-resistant gram-negative coccobacillus.\(^2\) Ab has the ability to form biofilms on non-viable surfaces, surviving through high temperatures as well as extended periods of desiccation, making it a very resilient pathogen. Therefore, due to its high persistence, pathogenesis, and multidrug resistance, this pathogen has been associated with skin and soft tissue infections, including necrotizing fasciitis, as well as lethal infections such as pneumo-

In the context of drug resistance acquired by Ab, the more common resistances are to carabepenem, β-lactams, rifampicin, and emerging strains against once successful colistin have been isolated.\(^7\) Ab typically acquires resistance via antimicrobial inactivating enzymes such as lactamases, mutations within the bacterial genome that alters antimicrobial targets, and horizontal transfer with interactions with other microorganisms.\(^7\) Given the increasing difficulty in treating Ab infections, and the high mortality rates associated to this evolving pathogen, there is an urgent need to understand its biology and mechanisms of pathogenesis.

Despite its clinical importance, relatively little is known about the innate host defense mechanisms against respiratory Ab infection. Similar to the neutrophil, the macrophage is another important phagocyte that is generally involved in host defense against pathogen invasion. These professional phagocytic cells are one of the first innate immune cells in the respiratory tract to be activated after infection, and function to detect and eliminate invading pathogens while activating the adaptive immune. Only recently, Qiu et al. showed that alveolar macrophages (AMs) are essential in the clearance and cellular immune response to Ab by microtubule- and microfilament-dependent phagocytosis.\(^11\) AMs upon stimulation produce elevated levels of pro-inflammatory cytokines upon stimulation, promoting the recruitment of neutrophils. Similarly, AMs produce high levels of nitric oxide (NO), an effector molecule that is important to combat Ab infection. However, it was unknown whether these mechanisms were present or altered in Ab infection in the presence or absence of alcohol abuse.

In the manuscript discussed here, for the first time, it has been proven that although macrophages are believed to play a relatively minor role in the overall host defense against Ab infection, they play an essential role in the initial stage of host defense against respiratory Ab infection, partially through an NO-dependent mechanism.\(^1\) In addition, an important effect of alcohol has been revealed in this study that explain, the majority of CAP-Ab infections and the impaired immune system observed in the individuals exposed to both Ab and alcohol consumption. Alcohol consumption is also correlated with impaired immune responses including AM dysfunction in phagocytosis, killing of bacteria, and cytokine secretion.\(^4\) However, there was no study available associating the direct effects of alcohol exposure on macrophage effector functions.

In this issue, Asplund et al. provide a proof-of-principle study suggesting that physiological alcohol concentrations impair macrophage antimicrobial functions against Ab using a J774.16 macrophage-like cell line. Alcohol-exposed macrophages shown...
this opportunistic microbe that has been underestimated as a serious threat for human health.

Disclosure of Potential Conflicts of Interest
No potential conflicts of interest were disclosed.

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