



An Old Solution for a New Problem: Antiserum against Emerging Infectious Diseases

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INTRODUCTION

Heterologous neutralizing serums or antiserums consist of neutralizing antibodies produced mainly in horses or sheep and have been effectively used for more than a century. Antiserums were born in the golden age of microbiology when, in 1890, von Behring and Kitasato showed that the serum of a diphtheria-infected animal confers immunity against the same disease on naive animals (1, 2). Four years later, antiserum was used in humans. From that point, this method has always been demonstrated to be highly effective in the treatment of both infection and envenoming. However, antiserums did not have good outcomes with respect to safety in their initial applications, causing many life-threatening side reactions (3). Currently, in many applications, heterologous serums have been replaced by other drugs, such as antibiotics or homologous serums. However, in the case of envenoming from snakebites, scorpions and arachnids, antiserums remain the only effective treatment (4). In recent applications, antiserums have demonstrated a good safety profile, with <15% of patients having mild adverse reactions and <1% having severe reactions (4–6). The only weakness antiserums have is that, like most biological products, the induced reactivity in patients generates antibodies against the antiserum (7). This weakness causes the effectiveness and safety to be compromised in successive treatments, or, in other words, heterologous serums can only be used once.

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HETEROLOGOUS SERUMS AS ANTIMICROBIALS

In the first decades of the twentieth century, before the advent of antibiotics, heterologous serums were the best treatment choice against infectious diseases (8, 9). Many diseases were treated with heterologous serum with high effectiveness but with variable safety. For example, in 1904, a *Neisseria meningitidis* epidemic in New York City was controlled with a heterologous specific serum, decreasing the mortality by one-third (10).

Later in the twentieth century, antiserums began to be displaced by drugs with better safety profiles, antibiotics, and vaccination. However, for the treatment of envenomation, tetanus, diphtheria, and rabies, antiserums have seen continued successful use. Currently, the treatment for tetanus and diphtheria has been changed from antiserums to homologous serums obtained from healthy human donors, but in many countries, antiserums remain the only option for such treatment. In the case of snakebite and other envenomations, the antiserum is the only effective treatment.

FROM NOW ONWARD

For many emerging diseases, such as the Ebola virus, the risk–benefit equation for the use of antiserum appears to be highly tilted toward benefit. Additionally, it is necessary to use the antiserum only once because surviving patients demonstrate immunity after first contact. Another benefit is the low production cost, which makes this type of drug affordable for most countries (6, 11, 12). Unfortunately, while vaccination, monoclonal and homologous antibodies became the most popular

solutions, antiserums had less success. Against many emerging diseases and future threats, however, antiserums could have a chance. Dixit and coworkers (6) are proposed antiserum as a possible solution to avian influenza, MERS-CoV, and viral hemorrhagic fevers. Heterologous serum also has the advantage that it can be made using recombinant proteins, which avoids the risk of manipulating the infective pathogen during the production stage.

CONCLUSION

Antiserums are an old drug with more than a century of use. Perhaps for this, most pharmaceutical companies and scientist

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