**Removal of Drug-Resistant Bacteria and Ebola Virus from Whole Blood with a Sorbent Hemoperfusion Device: Carbapenem-Resistant Enterobacteriaceae**

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**Introduction:** Many pathogenic bacteria and viruses invade the body by binding to specific regions on the surface of vascular endothelial cells. Heparan sulfate (HS) glycosaminoglycan is a common attachment site. We have developed a biomimetic adsorption media that captures many pathogens, toxins and pro-inflammatory cytokines within a disposable cartridge, during a dialysis-like extracorporeal therapy. Using covalently-bonded heparin, an analog of HS, together with supplemental adsorbents, we mimic receptor sites on human cell membranes while presenting a highly anti-thrombogenic blood-contacting surface. The single-use device (Fig. 1) has tens of square meters of active surface area and low priming volume. One potential clinical indication is as a supplement or alternative to anti-infective drugs in the prevention of sepsis, e.g., by early treatment of often fatal bloodstream infections caused by viruses and drug-resistant bacteria. Here we report the removal of carbapenem-resistant Enterobacteriaceae (‘CRE Superbugs’), and a rationale for removing Ebola virus, both of which cause bloodstream infections with mortality rates that can exceed 50%.

**Methods:** Heparinized UHMWPE beads were produced as described by Larm et al. The beads were rendered hydrophilic prior to surface coupling. Reactive amino functions were introduced, followed by a modified end-point attachment to the aminated surface of heparin by oxidative amination, utilizing the aldehyde function in the reducing terminal residue of partially (nitrous acid) degraded native heparin. The resulting PE-beads, with covalently end-point attached heparin, were sterilized with ethylene oxide.

**Results and Discussion:** We have previously reported methicillin-resistant *Staph. aureus* (MRSA) removal from whole human blood averaging 71% reduction with a single pass. One option is to administer hemoperfusion therapy in a dialysis session (Fig. 1) during which the patient’s entire circulating blood volume is typically subjected to 10-15 passes through the extracorporeal circuit, likely reducing bloodstream pathogen concentrations to undetectable levels. As shown in Table 1, both the efficiency of removal and the binding capacity of the media are very high. Therefore the use of this whole blood affinity therapy, optionally combined with anti-infective drugs (when available), should accelerate the clearance of blood-borne pathogens and toxins to a level that can be handled by the patient’s immune system. It is expected that reducing the pathogen load and shortening the duration of CRE bacteremia and Ebola viremia will significantly improve outcomes. When the pathogen and/or the site of the infection are unknown, a safe, broad-spectrum affinity therapy should delay the progression from bacteremia to septic shock and multi-organ failure, allowing more time for diagnosis and treatment.

**References:**
1. Bartlett, A.H., Park, P.W. in Glycans in Diseases and Therapeutics, Berlin: Springer-Verlag, 2011, p.31

**Table 1.** In vitro binding to heparin-functional media showing high efficiency of removal and high binding capacity per gram of adsorption media: typical bacteria concentration during bacteremia is ca. $10^9$ to $10^7$ CFU/mL (in 5 liters of blood.)

<table>
<thead>
<tr>
<th>Test Medium</th>
<th>Starting Concentration (CFU/ml)</th>
<th>% Removed</th>
<th>Capacity (CFU/g media)</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli ATCC 8739</td>
<td>6.15E+05</td>
<td>99.75</td>
<td>2.04E+06</td>
</tr>
<tr>
<td>K. pneumoniae ATCC 13883</td>
<td>4.02E+05</td>
<td>36.43</td>
<td>4.88E+05</td>
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<tr>
<td>E. coli ATCC BAA-2606 (CF)</td>
<td>2.57E+05</td>
<td>99.99</td>
<td>8.56E+05</td>
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<tr>
<td>K. pneumoniae ATCC BAA-2614 (CF)</td>
<td>1.40E+05</td>
<td>99.94</td>
<td>4.66E+05</td>
</tr>
</tbody>
</table>

**Figure 1.** Seraph® Microbind® Affinity Blood Filter, (ExThera Medical Corp., Berkeley, CA) in series with a dialyzer.