Neisseria gonorrhoeae is the cause of the second most common sexually transmitted infection, with approximately 80 million new cases of gonorrhea reported annually. The recent emergence of clinical isolates resistant to the last monotherapy against this bacterium, the cephalosporins, illustrates the need for new anti-gonococcal agents. We recently identified resazurin, a commonly used viability dye, as a novel antibacterial agent against N. gonorrhoeae. While resazurin exhibited potent in vitro antimicrobial activity, in vivo, resazurin did not limit the colonization of mice with N. gonorrhoeae following vaginal infection. The ineffectiveness of resazurin in vivo is likely due to its interaction with serum albumin which completely diminishes its antimicrobial activity. Treatment of mice with a resazurin analog that maintains its antimicrobial activity in the presence of serum albumin, resorufin pentyl ether, however, approached a significant decrease in the percentage of mice vaginally colonized. This treatment also decreased vaginal colonization by N. gonorrhoeae over time. Together, these data suggest resazurin derivatives have potential for the treatment of gonorrhea. Current investigations in the laboratory are focused on the mechanism of action of these compounds which appears to be linked to the lipoprotein sorting system of this bacterium. (Supported by NIH Grant P20GM103434 to the West Virginia IDeA Network for Biomedical Research Excellence, a grant from NIH-NIAID [5K22AI087703], and funding from WV-NASA).