

Bicarbonate-Supplemented Media for Antibiotic Susceptibility Testing of MRSA [LAB0206]

Background

- *Staphylococcus aureus* is a serious community and nosocomial pathogen, and a leading cause of bacteremia, infective endocarditis, and device-related infections.
- Many of these infections are caused by methicillin-resistant *S. aureus* (MRSA), which causes more than **15,000 deaths in the U.S. each year**.
- **Treatment for MRSA generally involves the use of costly and/or toxic drugs**, including vancomycin, daptomycin, and fifth generation cephalosporins, such as ceftaroline.
- **β -lactams (penicillin-like agents) are less toxic and cheaper** but available antibiotic susceptibility tests using standard lab media uniformly identify all MRSA strains as resistant to β -lactams.
- **International guideline committees, such as the IDSA, recommend not to use β -lactams to treat such infections.**
- **However, recent studies show that standard *in vitro* β -lactam antimicrobial resistance in MRSA may not always correlate to therapeutic efficacy *in vivo*.**
- A test that is capable of accurately determining if select MRSA strains are susceptible to treatment with β -lactams would be both medically and economically beneficial to patients and the healthcare system.

Innovation

- **Dr. Arnold Bayer has developed a bicarbonate-supplemented media that can accurately detect the susceptibility of select MRSA strains to early generation, standard-of-care β -lactams, including cefazolin (CFZ) and oxacillin (OXA).**
- Sodium bicarbonate (NaHCO_3), the body's primary biological buffer, plays a critical role in the susceptibility of *S. aureus* to various antibiotics, including β -lactams.
- Dr. Bayer's media increases detection of susceptibility in select MRSA strains to β -lactams, which he terms " NaHCO_3 -responsive" strains.
- Importantly, *in vitro* susceptibility to β -lactams as predicted by the bicarbonate-supplemented media translates and predicts susceptibility to β -lactam therapy in endovascular infection models *in vivo* (e.g., experimental endocarditis).
- **Stage of development**: The ability to predict MRSA susceptibility to β -lactams using bicarbonate-supplemented media has been validated in a rabbit model of infective endocarditis and tested against a large set of clinical MRSA bloodstream isolates.
 - " NaHCO_3 -responsive" MRSA strains, as predicted using the bicarbonate-supplemented media, were often highly susceptible to β -lactams *in vivo*.
 - In clinical MRSA bloodstream samples, 75% and 36% of isolates displayed the NaHCO_3 -responsiveness phenotype to the prototype β -lactams, cefazolin and oxacillin, respectively.

Advantage

- The modified media can determine if a patient infected with a particular MRSA strain might be treatable with less toxic and/or cheaper antibiotics.

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Applications

- Determine susceptibility of MRSA to certain β -lactam antibiotics.

Lead Inventor: Arnold Bayer, MD

Related Publications

- Rose WE, Bienvenida AM, Xiong YQ, Chambers HF, Bayer AS, Ersoy SC. Ability of bicarbonate supplementation to sensitize selected methicillin-resistant *Staphylococcus aureus* strains to β -lactam antibiotics in an ex vivo simulated endocardial vegetation model. *Antimicrob Agents Chemother.* 2020; 64(3).
- Ersoy SC, Otmishi M, Milan VT, et al. Scope and predictive genetic/phenotypic signatures of bicarbonate (NaHCO_3) responsiveness and β -lactam sensitization in methicillin-resistant *Staphylococcus aureus*. *Antimicrob Agents Chemother.* 2020; 64(5).
- Ersoy SC, Abdelhady W, Li L, Chambers HF, Xiong YQ, Bayer AS. Bicarbonate resensitization of methicillin-resistant *Staphylococcus aureus* to β -lactam antibiotics. *Antimicrob Agents Chemother.* 2019;63(7).
- Selvi C Ersoy , Adhar C Manna, Richard A Proctor, Henry F Chambers , Ewan M Harrison , Arnold S Bayer, Ambrose Cheung. The NaHCO_3 -Responsive Phenotype in Methicillin-Resistant *Staphylococcus aureus* (MRSA) Is Influenced by *mecA* Genotype. DOI: 10.1128/aac.00252-22
- Selvi C Ersoy, Barbara Gonçalves, Gonçalo Cavaco, Adhar C Manna, Rita G Sobral, Cynthia C Nast, Richard A Proctor, Henry F Chambers, Ambrose Cheung, Arnold S Bayer. Influence of Sodium Bicarbonate on Wall Teichoic Acid Synthesis and β -Lactam Sensitization in NaHCO_3 -Responsive and Nonresponsive Methicillin-Resistant *Staphylococcus aureus*. DOI: 10.1128/spectrum.03422-22.
- Sook-Ha Fan, Richard A Proctor, Selvi C Ersoy, Adhar C Manna, Ambrose L Cheung, Friedrich Götz, Henry F Chambers, Arnold S Bayer. Role of the NaHCO_3 Transporter MpsABC in the NaHCO_3 - β -Lactam-Responsive Phenotype in Methicillin-Resistant *Staphylococcus aureus*. DOI: 10.1128/spectrum.00141-23.
- Warren E Rose, Ana M Bienvenida, Yan Q Xiong, Henry F Chambers, Arnold S Bayer, Selvi C Ersoy. Ability of Bicarbonate Supplementation To Sensitize Selected Methicillin-Resistant *Staphylococcus aureus* Strains to β -Lactam Antibiotics in an Ex Vivo Simulated Endocardial Vegetation Model. DOI: 10.1128/AAC.02072-19