Aminoglycoside Resistance in Enterobacteriaceae and Pseudomonas aeruginosa

**What are aminoglycosides?**

Aminoglycosides are bactericidal antimicrobial agents that are used to treat a variety of severe infections, usually in combination with b-lactam agents. Aminoglycosides have low gastrointestinal absorption. Patients treated with aminoglycosides must be closely monitored because of the potential toxicity associated with their use.

The target of aminoglycoside activity in the bacterial cell is the 30S ribosomal subunit. When the drug binds to the ribosome, the structure is unable to translate mRNA for protein production, leading to cell death.

Aminoglycosides used for treatment of infections caused by *Enterobacteriaceae* or *P. aeruginosa* include gentamicin, amikacin, netilmicin, and tobramycin. In the United States, gentamicin is the most commonly used aminoglycoside.

**How many aminoglycosides should a clinical laboratory test and report?**

Testing depends on the drugs most commonly used in the hospital. However, gentamicin and either tobramycin or amikacin are typically on many commercial panels. For testing and reporting strategies, please consult the National Committee for Clinical Laboratory Standards (NCCLS) approved standard document M100-S9 (1).

**What causes resistance to aminoglycosides?**

Aminoglycoside resistance is caused by the presence of one or more of the following mechanisms: inactivation of the drug by aminoglycoside-modifying enzymes (AMEs) produced by the bacteria, ribosomal alterations that prevent the drug from binding to its site of action, or loss of permeability of the bacterial cell to the drug. Genes that encode for AMEs, the most common mechanisms of resistance, can be passed from organism to organism on plasmids and transposons.

**Does resistance to one aminoglycoside predict resistance to the others?**

Not necessarily. AMEs vary in their drug specificity, and many organisms can produce one or more AMEs. In addition, most AMEs inactivate more than one aminoglycoside. Therefore, resistance to one aminoglycoside may not predict resistance to the others.

**Is resistance to aminoglycosides common among gram-negative bacilli?**

In general, resistance is relatively common in *P. aeruginosa* but less common in *Enterobacteriaceae*. *Enterobacteriaceae* resistant to gentamicin and tobramycin can be susceptible to amikacin or netilmicin because these drugs are not affected by many of the AMEs. Therefore, the prevalence of amikacin resistance can be lower than the prevalence of resistance to gentamicin and tobramycin, depending upon the resistance mechanisms present at a healthcare facility.

*Enterobacteriaceae* have greater susceptibility to aminoglycosides than do isolates of *P. aeruginosa* because efflux and permeability mechanisms are more common in the latter organism.
Should *Salmonella* spp. and *Shigella* spp. be tested against aminoglycosides?

Aminoglycosides are not clinically effective against *Salmonella* species and *Shigella* species, although they may appear susceptible in vitro (1). NCCLS guidelines recommend that for these isolates aminoglycosides should not be tested or reported.

**Between aminoglycosides, why are the zone sizes and MICs different within the susceptible, intermediate, and resistant breakpoints?**

NCCLS guidelines outline susceptible, intermediate, and resistant breakpoints for the aminoglycosides used to treat infections caused by *Enterobacteriaceae* or *P. aeruginosa* (1). Zone size and minimum inhibitory concentration (MIC) breakpoints are determined by reviewing each drug’s pharmacokinetics, pharmacodynamics, population distributions, and clinical efficacy at different MICs and zone diameters. Therefore, breakpoints differ by drug.


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