What do you view as the most important problem with regard to diagnosis and treatment of multidrug-resistant Gram-negative bacilli?

[350 respondents provided an answer to this question; some answered in > 1 category below]

**Lack of antimicrobials/ Need for NEW DRUGS** [mentioned by 179 respondents]
- Lack of new drugs / good agents / running out of antimicrobial options [by 179]
- Lack of drug development to keep pace with resistance development [MN]
- We do not have aztreonam, IV Bactrim, amikacin available and no new antibiotics on the way for gram negatives. [LA]
- Amikacin shortage specifically mentioned by 10 respondents, e.g., “Amikacin shortage has complicated treatment as some of the isolates were only susceptible to it”
- We need IV fosfomycin. [IL]
- Toxicity of current antimicrobials and need for non-toxic safe agents effective against MDR GNB mentioned by 15 respondents
- Once daily treatment for *P. aeruginosa* - without this, it is very difficult to treat as an outpatient unless there is quinolone susceptibility or with renal dysfunction to dose cefepime once a day; Aminoglycosides are a little scary. [FL]

**Diagnostic / Clinical lab issues** [mentioned by 103 respondents]
- Poor performance of automated MIC methods / variability in MIC testing / need accurate susceptibilities / accurate detection of KPC and ESBLs mentioned by 29 respondents, e.g., “Detection with automated equipment remains a challenge, especially with inducible resistance”, “Need rapid, reliable, and reproducible laboratory testing”, “Lack of reproducibility (precision) of breakpoints determined by automated MIC methods (Vitek, Microscan)and even E-test”
- Problems with a delay in identification and susceptibility results / need for more rapid identification and susceptibility data mentioned by 25 respondents, e.g., “Rapid identification of presence of ESBLs and inability to rapidly distinguish between mechanisms”
- Uncertain / poor correlation between the in vitro susceptibility results and clinical outcome mentioned by 13 respondents, e.g., “Which antibiotics are predicted to work nor not based on these tests?”
- Need for availability of panels in the US mentioned by 8 respondents, e.g., “Diagnosis is hindered by Microscan panels that do not provide the MICs at the new, lower breakpoints for certain drugs”, “Delay in automated FDA approved diagnostics will cost micro labs additional expenditures that financially strapped institutions are ill prepared to incur.” “Most labs can not and will not manually test all isolates. Until the major automated systems change the breakpoints on their panels the CLSI changes are pointless.”
- Confusion as to nomenclature of ESBLs, lack of knowledge regarding implication of an ESBL. [MN]
• The current lack of a rapid (ie, PCR) probe for MDRO Pseudomonas and MDRO Acinetobacter baumannii. [NC]

• Communication issues between laboratory and clinician mentioned by 4 respondents, e.g., “Lack of interest in our microbiology lab as to the clinical importance for the physicians caring for the patients. Unwillingness of lab to communicate with physicians.”

• The difficulty in establishing presence of carbapenem resistance, due to changing breakpoints, different reliability of methods, expertise needed to do Hodge test etc. We currently use ertapenem MIC as a screen with Hodge test and PCR to look for carbapenemases, but will adopt new CLSI guidelines. Luckily, CRE remain rare in our hospital (and city) with porin-mutant pseudomonas a larger problem. [UT]

• New breakpoints will not be helpful. It may paradoxically drive use of antibiotics in different directions and fuel additional resistance. There will be less emphasis on defining mechanisms of resistance (ESBL vs. AmpC, etc) and a greater tendency to just broadly classify all as resistant to B-lactams. [NE]

• No good NCCLS criteria for tigecycline [IL]

• Prior teaching that if an organism is an ESBL then carbapenems are the drugs of choice- now we will not know if ESBLs. If we use the new lower breakpoints, are we safe to ignore the prior teaching?? We just had a meeting of our division today on this very issue- we need guidance! [ME]

• ID division here plans to meet to discuss new breakpoints and whether to start using them [PA]

• How many MDR gram negatives we are missing. I had problems with ertapenem resistance (not in Pseudomonas that is obviously not susceptible) when the isolate was imipenem susceptible. The ertapenem is not usually shown in our antibiogram and I had treated an ertapenem resistant/imipenem susceptible organism with ertapenem presuming that there was class susceptibility. Since then, we reviewed our antibiogram and we found that ertapenem is not as active as the other carbapenems for traditionally though-to-be susceptible organism (Klebs, E. coli, Citrobacter, etc). [SC]

• As I was unable to answer question 4 with the choices give, I have summarized our current approach. Based on review of our internal data, we have found that an isolate with a CTAZ MIC > 4 OR CTX MIC > 1 has a sensitivity and specificity of detecting ESBL of > 99% with laboratory-confirmed ESBL as the gold standard, so feel reasonably reassured that we have surrogate means of identifying ESBL producers for infection control surveillance if we do away with the screen. There was some concern expressed by our group regarding the reporting of pip-tazo and cefepime susceptibilities. In adult inpatients, among 80 ceftriaxone-nonsusceptible isolates, about 75% of these would be pip-tazo and cefepime susceptible. Previously, these susceptibilities would have not been reported in patients with sterile site infections due to ESBL and hence the clinician would have been directed to use a carbapenem. As there was some concern expressed that cefepime or pip-tazo (as opposed to a carbapenem) would not provide adequate treatment of serious invasive infections due to ESBL, the decision was made to take a more conservative approach similar to prior guidelines. Additionally, it was suggested that when carbapenem is reported for sterile site isolates, only ertapenem be released unless the MIC interpretation is intermediate or resistant in which case meropenem should be released as well. Ultimately, we feel that further clinical data is needed to confirm that non-carbapenems are adequate for treatment of invasive infections due to isolates that would previously have been labeled as ESBL given previously published data suggesting worse outcomes in those patients treated with non-carbapenems with ESBL bloodstream infections. [CA]

• Confusing terminology, where ESBL is but a subset of the MDRO, and seems to be an arbitrary designation rather than a serviceable description. [CA]
• Lack of any information about unusual susceptibility results for MDR GNR's. For example, had case of persistent Klebsiella peritonitis due to probable KPC producing organism that repeatedly tested susceptible for Bactrim. I asked several "experts" and even sent out a query on EIN asking whether one would use Bactrim. Is this a plausible antibiogram? Is this sort of like ciprofloxacin with ESBL organisms that higher treatment failure rates than expected based on in vitro susceptibility? Could not any substantive answers from anybody. [PA]

• While the attachment gives new CLSI breakpoints for cephalosporins, it does not give the new CLSI guidelines for carbapenem interpretation, which are different than those published in the Jan 2010 CLSI guidelines (M100-S20). These newer guidelines were publicized in an audioconference, and are on the CLSI website for the Jan 2010 meeting minutes: http://tinyurl.com/carbapenem. It's not clear to me how widely these have been disseminated, or are being used. [PA]

**Antimicrobial stewardship / overuse and proper use of antibiotics** [mentioned by 24 respondents]
- Antibiotic restriction is key / antimicrobial stewardship **mentioned by 4 respondents**
- Overuse of antibiotics by non-ID trained physicians. If something is NOT done to stop overuse in ICUs we are in trouble. [OH]
- Overuse of antibiotics in long-term care settings **mentioned by 5 respondents**, e.g., “repeated courses of antibiotics in residents of long-term health care facilities usually with poor evidence for infection vs colonization”
- We believe that the overuse of carbapenems is the single greatest problem behind what we are now faced with. The introduction of a newer agent or agents now will only repeat the cycle of overuse-> resistance unless hospitals can place very very aggressive restrictions on the use of these agents. [NJ]
- Lack of education in medical school and residencies about proper use of antimicrobials and antimicrobial stewardship. [PA]
- Tigecycline is almost useless as monotherapy, but only ID clinicians seem to understand that [MD]

**Treating colonization / Recognizing infection** [mentioned by 23 respondents]
- Over-treatment of colonization **mentioned by 24 respondents**
- Identifying a pathogenic role versus colonizing role is almost as important as having additional agents [NY]
- In many instances there is difficulty in differentiating colonization vs infection. [NE]
- Often recurring treatment of GNR's in urine, wound, or sputum specimens when no apparent active infection is in need of treatment [CA]

**Optimal treatment unknown / Need for clinical trials or guidelines** [mentioned by 22 respondents]
- Lack of information on use of combination therapy **mentioned by 8 respondents**
- Questions of synergy. Does using a carbapenem with colistin make sense if isolate is resistant to carbapenem by itself. Is tigecycline useful in combination therapy if blood stream infection (NOT as solo agent since serum levels are low with tigecycline) [NJ]
- Limited information regarding utility of combination therapy with drugs to which the isolate is resistant on standard susceptibility testing **mentioned by 2 respondents**
- Still not sure if isolates resistant to imipenem might be susceptible to doripenem (this testing takes longer but some turn up sensitive). Are 2 drugs better than one? [CO]
• Absence of guidelines for treatment of MDR GNR especially when the GNR is panresistant. [WI]
• The biggest problem I see with MDR is the over-treatment of wounds - especially decubiti with or/without osteomyelitis, often as recommended by other infectious diseases physicians. I think the IDSA urgently needs to get a clinical practice guideline that looks at the evidence for treatment of wounds/sacral osteo - and advocates limited 1-2 week courses of therapy if debridement has been adequate and/or there's no hope for cure. I think the ID community is doing a lot of collateral damage in the way they over-treat these patients - many of winding up in longterm, acute care. [TX]

• Reliability of BLICs; lack of papers outlining success with 2nd-3rd line agents [WI]
• Tigecycline useless for Acinetobacter (patients break through with bacteremia while on it). Lack of data if combination therapy beta-lactam / carbapenem + colistin is better than monotherapy and for how long to treat to avoid relapse [FL]
• No data on relative efficacy of tigecycline versus colistin [OH]
• Lack of clear guidelines for optimal treatment (some evidence--albeit animal models, in vitro and scant retrospective clinical--supports combining carbapenems with another active agent such as colistin or aminoglycoside for KPC Klebsiella). This option has not been widely disseminated [PA]
• Deciding which of the 3 drugs used for MDR Acinetobacter (Unasyn, Colistin and Tigecycline) should be used to treat such an infection and in what combination, based on the disk size or MIC. [LA]
• The lack of data on clinical outcomes with treatment using beta-lactams or BL/BLI combinations in patients infected by ESBL-positive strains showing susceptible MICs [WA]

Infection control and prevention [mentioned by 20 respondents]
• Isolation and infection control mentioned by 20 respondents
• It is also not clear what to isolate. The more you isolate the less compliant folks are. I am glad with these new guidelines-because they are not rationale for isolation. Our lab director thinks we should isolate all AmpCs. We have recently decided to isolate pts who we can’t find 2 abx classes to treat. We are not doing a good job isolating ESBLs. A # of abx approach will help in dealing with new guidelines. [MA]
• Lack of infection prevention, abx stewardship, and lack of drugs. All our problems are clearly linked to transmission in healthcare setting mainly in the rehab or LTCF setting. [LA]
• Prevention! Reducing overall antimicrobial use, infection control, etc. [WA]
• Poor hand hygiene leading to spread of the organisms, and patients hospitalized for >3 months (many of whom have no hope for meaningful survival) who get recurrent nosocomial infections. We are selecting for pan resistant organisms for which no antibiotic treatment is available. [NY]
• Unclear when to isolate patients --where on the rheostat of resistance is the threshold at which we should isolate. We made up our own rules. [MD]
• Difficulty in eradicating the carrier/ colonization status, 100% compliance with contact isolation which is the most essential step in disease prevention rarely happens even in the best of the centers [NY]

Comments about colistin / polymyxins [mentioned by 10 respondents]
• Dosing of colistin is still not clear and limited options other than colistin mentioned by 4 respondents
• Optimal dosing/route of administration of colistin (for MDR pneumonia)? [MI]
• Lack of availability of information on polymixin B sensitivity [OH]
• Lack of routine method for colistin susceptibility testing. We use turbidity in 4 mcg/mL identification well from our Gram negative Microscan panels as a rough gauge, for example. Not sure how Kosher this is [PA]
• I hate practicing 1950s medicine by resorting to colistin, with its lack of trials and worrisome side effect profile. [OK]
• Side effects limiting use of colistin most elderly patients. [TX]
• We are left with colistin. While tigecycline is available, I have yet to find a MDR isolate (Enterobacter, Pseudomonas, etc) that is susceptible. [IN]

**Pediatric-specific comments** [mentioned by 8 respondents]
• Treatment options more limited in children mentioned by 6 respondents
• Per discussion at our P&T mtg this week, CLSI breakpoints and other federal agencies governing testing/therapy are not currently in alignment. In children - limited number of agents appropriately evaluated to be used for treatment [GA]
• 1. We are very fortunate in our Peds Units that we have not had carbapenemase producers (but it is on the adult units). 2. ESBL uncommon but so far universally S to carbapenems. 3. We do have drug resistance with Pseudomonas, fortunately none to tobra (yet). Part of our issue here is our pulmonologist likes to treat colonization with monotherapy and due to this is creating more interesting challenges for us. I get rare questions from a local long term facility regarding these children and am usually successful in getting children off the un-needed antimicrobials, which has helped some. But our day is coming... [NC]
• Compliance with the guidelines, awareness of community pediatricians of the emerging resistant GNR and the treatment options. Excessive use of cephalosporins third generation in all clinical settings regardless of cause. [NY]
• The lack of consensus on how best to treat multi-drug resistant gram negative infections especially in pediatrics (I have had to ask adult ID colleagues how best to treat some of these infections), the increasing numbers of pediatric patients from long term care facilities that are colonized with MDR GNRs who need admission to an acute care hospital [PA]

**Miscellaneous comments** [mentioned by 15 respondents]
• Lack of consistent knowledge in labs and MDs [CA]
• Our society's inability to deal with death and dying issues, evidenced by a too frequent choice of very aggressive and expensive care being given to moribund, unresponsive and unsalvageable patients. [IL]
• Being sure there is significant education of care providers about interpretation of new breakpoints, ESBL, need for isolation, etc. [WY]
• The continued evolution w/ increasing resistance w/ expectations that tomorrow will be worse. [FL]
• Being consulted in a timely manner. [MN]
• Lack of knowledge of physicians about problem [CA]
• Aside from emergence, confusion. This is going to challenge primary care docs and to lesser extent ID docs. [MN]
• Every patient with a serious Gram-negative infection should get an ID consult [OH]
• Lack of Medicare coverage for the more complex treatments as outpts [MT]
• New break points will require a lot of education before ID community can be comfortable [CA]
• When new break points are introduced, it is difficult to justify further testing to confirm existence of epidemiologically important CREs. Institutions unwilling to send out epidemiologically linked isolates. [CA]
• Non-expert clinicians trying to treat them without consultation from ID colleagues [PA]
• The SNF and LTAC breeding grounds for resistant organisms. [CA]