GLOBAL INFECTIOUS DISEASES INITIATIVE

TOPIC:

MULTI DRUG RESISTANT ORGANISMS CLINICAL IMPLICATIONS AND OUTCOMES

4th Lecture

October 9th, 2024

MARCELLINA'S PLACE
36 Isaac John Street, Ikeja, GRA. Lagos

CONVENER'S

OPENING ADDRESS

DR. FOLARIN ADEGBOYEGA OLUBOWALE
MD/CEO Global Infectious Diseases Initiative

It is with a great sense of satisfaction that I write for the final edition of our initiative event in Lagos.
I started this journey in the USA in 2007 and had the final edition in December 2023.

I am glad that I had the opportunity to bring home this event for at least 4 times in the last five years.

I had and still have the vision to raise the awareness of the specialty of infectious diseases in our country.

The Telemedicine program for Infectious Diseases I had the dream of establishing at my Alma Mata unfortunately did not live up to my expectations for various reasons.

I hope in the future that such a program that will benefit the patients and the health professionals will be given more serious attention in our country.

This year, we chose to discuss the importance of multidrug resistance organisms as a global problem to bring to the healthcare community about this very important problem facing the world.

I thank all that have supported our initiative efforts over the years.

May the good Lord bless all our efforts.

Dr Folarin Adegboyega Olubowale

Program OF EVENTS

8:45AM	Welcome Address and Introductory Lecture. **Folarin Olubowale, MD**
9:00AM-9:30AM (ZOOM)	History of Antibiotics and the Emergence of Antibiotic Resistance. **Dr Chinelo Animalu**
9:35AM-10:05AM	Microbiology of Multidrugresistance In Nigeria: Progress And Challenges. **Prof Oyin Oduyebo**
10:10AM-10:40AM	Multidrug Resistance, A Major Biosecurity Threat to Lagos State. **Prof Akin Abayomi,** Lagos State Health Commissioner
10:40AM-11:00AM	Q&A
11:05AM-11:35AM	Navigating Multidrug (MDR) Infections: From Antibiotic Stewardship to Innovative Therapies. **Dr Folake Kofo Idowu**
11:40AM-12:10PM	Antibiotic Resistance In The Intensive Care Unit In Nigeria: Challenges And Strategic Approaches. **Dr Babaseyi Oyesola**
12:15PM-12:35PM (ZOOM)	Mdr Gram Negative Organisms: The Impact of Clinical Microbiology On Antibiotic Selection. **Dr Deanne Tabb**
12:40PM-1:10PM (ZOOM)	Resistant Gram Negative Bacteria As Agents of Bioterrorism. **Dr Bolaji Ogunsakin**
1:15PM-1:30PM	Q&A
1:30PM TILL DONE	Lunch&Light entertainment

SPEAKERS PROFILE

AKIN ABAYOMI, (OON)

Hon. Commissioner for Health, Lagos State

Professor Akin Abayomi is a specialist in Internal Medicine, Haematology, Biosecurity and Environmental health. He received his First degree in Medicine in the University of London, with fellowships from both Royal College of Medicine and Pathology in the United Kingdom and the College of Medicine of South Africa respectively. He also has a Master's in environmental Ecology from the University of Pretoria in South Africa.

Akin Abayomi has been exposed to a vast variety of geographical variations in disease patterns within the field of Internal Medicine and Haematology having worked in the UK, Nigeria, the Middle East, the West Indies, Zimbabwe and South Africa.

Professor Akin Abayomi is serving a second 4 year term as the Honourable Commissioner for Health in Lagos State, Nigeria in the Lagos State Executive Cabinet of His Excellency Governor Babajide Sanwo-Olu.

Prior to this Akin Abayomi was Professor of Medicine at the Nigerian Institute of Medical Research in Lagos, Nigeria and before that the Chief Pathologist and Head of the Division of Haematology at the University of Stellenbosch's Faculty of Medicine Science in Cape Town, South Africa.

Akin Abayomi has published over 70 scientific peer reviewed articles and book chapters in his medical career.

Professor Akin Abayomi is the Founder of the Global Emerging Pathogen Consortium also known as GET-Africa, which was entrenched at the peak of the Ebola outbreak in Lagos to address Biosecurity concerns in Africa. He is also the Honorary Professor to the Centre for Biosecurity Studies, University of the West Indies. Cave hill Campus, Barbados, Caribbean.

Prof. Abayomi is a fellow of the African Academy of Science and a recipient of the National Productivity Order of Merit Award (NPOM) and an Officer of the Order of the Niger (OON) as conferred by the President of the Federal Republic of Nigeria in recognition of his excellence in the field of medicine and his high productivity especially in the role he played in the expert containment of the COVID pandemic in Nigeria.

Professor Akin Abayomi plays Lawn tennis, rides horses and in his more agile years played Polo for the Kaduna and Ibadan Polo club. He is an avid environmentalist and maintains a large nature conservation called “The Emerald Forest Reserve” situated at Ikoyi Osun near Ashejire dam on the banks of the Osun River.

CONVENER'S PROFILE

DR. FOLARIN ADEGBOYEGA OLUBOWALE

MD/CEO Global Infectious Diseases Initiative

Dr. Folarin Adegboyega Olubowale was born in Ibadan, Nigeria in 1960 to the Late Chief & Mrs. Obayomi Olubowale, who both worked as nurses.

The earliest parts of his education were spent at a variety of schools due to his mother's work transfers to various parts of Nigeria. In 1972, he was admitted to Government College Ibadan, where he completed his WASC and his USC before being admitted to the College of Medicine at the University of Lagos (UNILAG) and graduating in 1983 with an M.B.B.S.

After serving at various medical facilities in Lagos, Nigeria, Dr. Olubowale proceeded to the United States in 1989. He completed his Internal Medicine residency at the Englewood Hospital (an affiliate of the Mount Sinai School of Medicine) in New Jersey in 1994. Dr. Olubowale completed his fellowship in Infectious Diseases in 1996, and during this time he met his wife Mrs. Folasade Olubowale, who currently is a registered pharmacist.

They are blessed with 3 children: Olayemi, Adeleye, and Omolade. Olayemi has completed his bachelor's degree at Georgia Tech, and is currently working towards his Master's degree at Vanderbilt University before he continues on to medical school. Adeleye is a rising senior at the University of Georgia, majoring in finance. Omolade, a rising sophomore at the University of Pittsburgh, is dual majoring in psychology and sociology before she continues on to a career in medicine, as well.

Dr. Olubowale established his Infectious Diseases practice in Columbus, GA. in 1997 and the rest is history. Medical Education has always been a passion of his, and in 2007 he held his first inaugural "Infectious Diseases Annual Lecture" for the healthcare providers of Columbus, GA. The event has only grown in relevance since its inception, with providers from neighboring states making appearances regularly.

Dr. Olubowale aims to extend this event to all corners of the globe, but first to Nigeria, his home country. The Global Infectious Diseases Initiative Inc. a charitable organization was formed to achieve this goal he set forth.

The first event was held on July 7th, 2017 in Lagos, Nigeria and featured speakers from the United States, along with dignitaries from his alma mater, UNILAG. This is the primary step to establishing an Infectious Disease Center in Lagos and partnering with local collaborators in the future to bring world-class care to the people. Dr. Olubowale and his family acknowledge that this is an ambitious project, but fully believe that with your help that all things are possible.

ANTIMICROBIALS

Humans Last Line of Defense

Dr Folarin Adegboyega Olubowale

What Are Antimicrobials?

4 Types of Antimicrobials:

1. **Antibiotics - treat Bacterial infection (e.g. Typhoid)**
   a. Target bacteria and they work by interfering with bacterial cell processes or structures.
   b. Ultimately lead to death or inhibition of bacterial growth.
   c. Examples: Penicillin, tetracycline, and erythromycin
2. **Antiviral - treat Viral infection (e.g. HIV)**
   a. Target viruses by inhibiting their replication and spread within the body.
   b. Treat viral infections such as influenza, HIV, and herpes.
   c. Examples: Acyclovir, oseltamivir, and ritonavir.
3. **Antiparasitic - treat Parasites (e.g. Malaria)**
   a. Target various stages of the parasite's life cycle, disrupting their growth and survival.
   b. Treat infections caused by parasites such as protozoa and helminths.
   c. Example: Chloroquine, albendazole, and ivermectin.
4. **Antifungal - treat Fungus infection (e.g. Thrush)**
   a. Target fungal cell membranes or interfere with fungal cell process to lead to death or inhibition of fungal growth.
   b. Agents used to treat fungal infections.
   c. Example: fluconazole, terbinafine, amphotericin B.

What Are Antimicrobials?

Antiseptics and Disinfectants

a. **Antiseptics: applied to living tissues to prevent infection**
b. **Disinfectants: used on inanimate objects and surfaces.**
c. **Examples: Alcohol-based hand sanitizers, hydrogen peroxide, and chlorine bleach.**

WORLD PUBLIC HEALTH ALERT

- **Micro-Organisms getting resistant to Drugs.**
  - **Infections not responding to treatment.**
- **Tuberculosis is now difficult to treat globally.**
- **HIV - Some babies are born with Drug Resistant HIV**

There has been an increased risk of dying from infections and increased spread of infections.

What Is Causing The Resistance to Drugs?

1. **Misuse/Overuse of these Medicine.**
2. **Poor Sanitation in certain places.**
3. **Poor Control of Medicine by Governments.**
4. **Natural changes to the Bacteria, Viruses, & Parasites or Fungus.**
5. **Lack of Health Awareness in the population.**

Do Not ABUSE ANTIMICROBIALS.

IT MIGHT COST YOU YOUR LIFE!!!

SPEAKER'S PROFILE

DR. CHINELO ANIMALU

MD, MPH, FIDSA

Dr Animalu is an Associate Professor of Medicine, division of Infectious Diseases at the University of Tennessee Health Science Center, Memphis. She is a product of the renowned College of Medicine, University of Nigeria, Enugu campus where she obtained her medical degree (MD/MBBS). She completed her internship and Internal medicine residency training at St Joseph hospital affiliated with University of Illinois, Chicago. She later obtained a master's degree in public health (MPH) from Tulane University, New Orleans.

Subsequently, Dr Animalu completed an Infectious disease fellowship program at the University of Tennessee Health Science Center, Memphis. She has been an infectious disease attending physician at Methodist University hospital, Memphis since 2015 till date and faculty member with College of Medicine UTHSC, Memphis from 2016 till date.

She is double board certified in Internal Medicine and Infectious Diseases. She is a fellow of the Infectious Disease Society of America (FIDSA) and fellow American College of Physicians (FACP). Her areas of interest are orthopedic infections, infection prevention and antimicrobial stewardship. She is well published in peer reviewed medical journals. She is actively involved in numerous mentoring activities in the College, especially among the minority community.

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GLOBAL INFECTIOUS DISEASE INITIATIVE
October 2024

MULTI DRUG RESISTANCE ORGANISMS
Clinical Implications And Outcomes

Chinelo Animalu MD, MPH, FIDSA
Associate Professor
Division of Infectious Diseases
College of Medicine, UTHSC, Memphis
Infectious Disease Specialist
Methodist University Hospital Memphis
October 2024

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History of Antibiotics and the Emergence of Antibiotics Resistance

No financial Disclosures

Objectives

- Discuss the history of antibiotics and emergence of antibiotics resistance
- Factors associated with the emergence of (multi drug resistant organisms (MDROs) in modern day era

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Brief Overview of Origin Of Antibiotics

- Sir Alexander Fleming is considered as the grandfather of antibiotics after he discovered penicillin while working on a fungus called Penicillium notatum. He noted that the fungus had destroyed bacteria in a staphylococcus culture plate. He successfully isolated the fungus substance called penicillin (PCN) in 1928.

Once PCN became widely available by 1940, a bacterial penicillinase was identified > resistant strains capable of inactivating the drug and as this became prevalent, synthetic studies were undertaken to modify penicillin chemically to prevent cleavage by penicillinases.

- In the case of streptomycin, introduced in 1944 for the treatment of tuberculosis (TB; "The Great White Plague"), mutant strains of *Mycobacterium tuberculosis* resistant to therapeutic concentrations of the antibiotic were found to arise during patient treatment.
- As other antibiotics have been discovered and introduced into clinical practice, a similar course of events has ensued.
- Over time of this antibiotic era, the number of identified resistance mechanisms, and their abundance, has increased at an alarming rate.

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Antibiotics background continued..

- Since the discovery of penicillin in 1928, many more novel classes of antibiotics have been discovered. Some were naturally-derived while others were synthetically derived basically between the 1950's and 1970's. Since then, newly marketed antibiotics are modification of the already-exiting classes
- As exciting as the discovery of newer classes of antibiotics is, it comes with a price. For the last decade, there has been increasing concerns about the emergence of organisms including bacteria, viruses, fungi and mycobacterium that have become resistant to the various classes of antimicrobials available.
- This concern has now grown to a full epidemic with more recent studies showing bacterial resistance to virtually all the classes of antibiotics available. These types of organisms are called multi-drug resistance organisms (MDRO) but commonly known in the general population as super-bugs.

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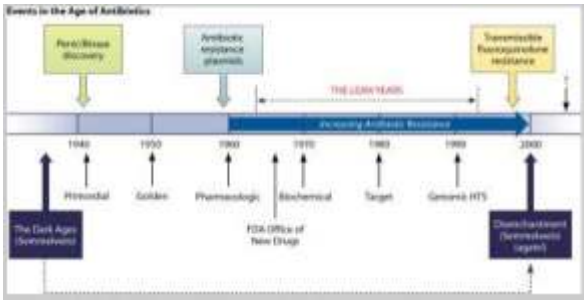
Events in the Age of antibiotics



The dark ages, the **preantibiotic era**; **primordial,** the advent of chemotherapy, via the sulfonamides; **golden,** years when most of the antibiotics used today were discovered**; the lean years**, the low point of new antibiotic discovery and development; **pharmacologic,** attempts were made to understand and improve the use of antibiotics by dosing, administration, etc.; **biochemical,** knowledge of the biochemical actions of antibiotics and resistance mechanisms led to chemical modification studies to avoid resistance; **target**, mode-of-action and genetic studies led to efforts to design new compounds; **genomic/HTS,** genome sequencing methodology was used to predict essential targets for incorporation into high-throughput screening assays; **disenchantment,** with the failure of the enormous investment in genome-based methods, many companies discontinued their discovery programs. Other milestones in this history include the creation of the **FDA Office of New** Drugs after the thalidomide disaster led to stricter requirements for drug safety, including the use of antibiotics. This slowed the registration of novel compounds. Before antibiotics were discovered, Semmelweis advocated hand washing as a way of avoiding infection; this practice is now strongly recommended as a method to prevent transmission

Origins and evolution of antibiotics resistance. (NIH.org)

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Factors associated with the emergence of MDROs in modern day era

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Factors associated with the emergence of MDROs in modern day era

- Excessive prescription of antibiotics has been identified as the major etiology of the emergence of these organisms > mostly through selective pressure exerted by the injudicious use of antimicrobials.
- Agricultural sector >
- wide use of pesticides.
- The mode of spread has been a major concern as well. The well recognized modes includes:

> The consumption of infected animal product

> Spread from food items like vegetables and fruits

> Person to person contact: Worse in healthcare settings.

Use of Antibiotics in agriculture and the risk to human health

- Routine use of antibiotics in agriculture has been described as a major contributor to the high occurrence of antibiotics resistance in human:
- Suspected mechanisms include:
- 1: Direct infection with resistant bacteria from an animal source
- 2: Breaches in the species barrier followed by sustained transmission in humans of resistant strains arising in livestock
- 3: Transfer of resistance genes from agriculture into human pathogens

- **Excessive prescription of antibiotics has been identified as the major etiology of the emergence of these organisms > mostly through selective pressure exerted by the injudicious use of antimicrobials.**

- **Tennessee ranks 5th in the nation for injudicious prescription of antibiotics in USA according to the CDC.**

- **In Nigeria and other parts of the world, other contributing factors include;**
- Healthcare environment factors such as lack of regulatory policies and infection control practices. Role of ASP, IPC.
- Lack of /availability of guidelines
- Patient pressure
- Limited knowledge about antibiotics and incorrect dosing practices by physicians, mid level providers and pharmacists.

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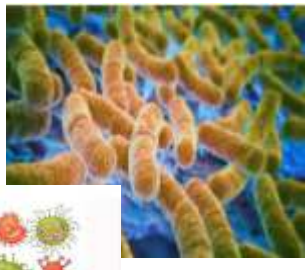
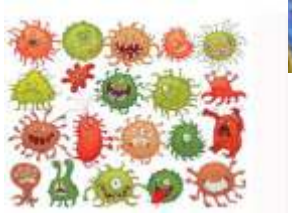
So, where does these prescribing trends lead us..

Creation of slippery little monsters

Super bugs

MDROs





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Super Bugs / MDROs

- The term "superbugs" refers to microbes with enhanced morbidity and mortality due to multiple mutations endowing high levels of resistance to the antibiotic classes specifically recommended for their treatment; the therapeutic options for these microbes are reduced, and periods of hospital care are extended and more costly. In some cases, super-resistant strains have also acquired increased virulence and enhanced transmissibility.
- The most dangerous of these organisms (MDROs or super bugs) have been found in the healthcare setting and spread is believed to be mainly from person-to-person contact.
- There has been conflicting studies about the role of healthcare workers in the transmission of these organisms from person to person leading to healthcare associated infections (HAI) through unintentional transmission of these organisms by person to person contact or through contaminated clothing like lab coats, scrubs and also by not following standard infection control measures like hand hygiene before after each patient contact, adhering to contact and special contact precautionary measures in patients who have already been diagnosed with one of these organisms·

Worse offenders in the

- **MRSA**
- **C difficile**
- **VRE**
- **CRE**
- **Most notorious mode of spread > HCW**
- **VISA**
- **VRSA**

Outbreaks

- There are instances of outbreaks of these organisms, some of which are MDROs in the communities but especially in the healthcare setting.
- There have been documented outbreak of these infections involving infected medical instruments and this has led to questions about the effectiveness of currently used disinfecting and cleaning techniques in healthcare settings.
- There was an outbreak of infections with carbapenemase resistant enterobacteriacae following exposure to duodenoscopes.

What is causing this resistance?

Overuse of Antimicrobials

Overuse of Antimicrobials

- CDC: > 50% Antimicrobials prescribed in US are unnecessary
  - Outpatient *and* Inpatient
  - ***Antimicrobials are the only medications where the use in one patient can compromise their efficacy in other patient.***
  - Use of metoprolol in Mr. and Mrs. Smith vs. Use of meropenem in Mr. and Mrs. Smith

Dellit et al. Clin Infect Dis. 2007;44:159-77

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How Long is Too Long?

- Brad Spellberg, MD
  - Compiled strong data (RCTs)
  - Consistently: Longer is not better

If Shorter is as good as Longer Duration, then why not cover the patient with antibiotics for longer?

Stewardship: Shorter = Better

Diagnosis	Short (d)	Long (d)	Result	#RCT
CAP	3-5	5-14	Equal	12
Atypical CAP	1	3	Equal	1
VAP	8	15	Equal	2
cUTI/Pyelo	5 or 7	10 or 14	Equal	9*
Intra-abd	4	10	Equal	2
GNB Bacteremia	7	14	Equal	3**
Cellulitis/Wound/Abscess	5-6	10	Equal	4†
Osteomyelitis	42	84	Equal	2
Osteo with Removed Implant	28	42	Equal	1
Debrided Diabetic Osteo	10-21	42-90	Equal	2‡
Septic Arthritis	14	28	Equal	1
AECB & Sinusitis	≤5	≥7	Equal	>25
Neutropenic Fever	AFx72 h	+ANC>500	Equal	1
P. vivax Malaria	7	14	Equal	1
Total: 14 Diseases				66 RCTs

*2 RCT included males, the smaller one found lower 10-18 d f/up cure in males with 7 days of therapy but no difference at longer follow-up, larger exclusive male study found no diff in cure; **GNB bacteremia also in UTI/cIAI RCTs; †3 RCTs equal, 1 (low dose oral flucox) ↑ relapses 2° endpoint; ‡all patients debrided, in 1 study total bone resection (clean margins); refs at https://www.bradspellberg.com/shorter-is-better

www.bradspellberg.com/shorter-is-better

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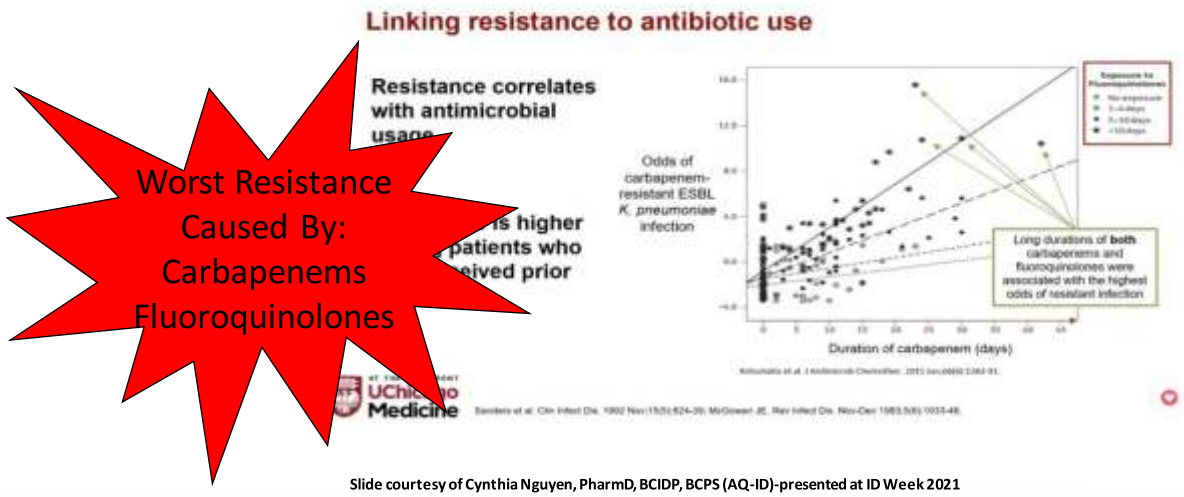
Longer Duration → More Resistance



Slide courtesy of Cynthia Nguyen, PharmD, BCIDP, BCPS (AQ-ID)-presented at ID Week 2021

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Worst Offenders for Resistance

	VRE	MRSA	ESBLs	CRE
2nd & 3rd Generation Cephalosporins	OR 5.9, p<0.001	RR 2.2, 95% CI 1.7-2.9	p=0.014	p=0.004
Fluoroquinolones	OR 1.6, p=0.03	RR 3.0, 95% CI 2.5-3.5	OR 11.2, 95% CI 1.9-63.2	
Carbapenems			p<0.0001	OR 14.97, p<0.001

Lautenbach E, et al. *Clin Infect Dis*. 2001 Oct 15;33(8):1288-94.
Ostrowsky BE, et al. *Arch Intern Med*. 1999 Jul12;159(13):1467-72.
Carmeli Y, et al. *Emerg Infect Dis*. 2002 Aug;8(8):802-7
Landman D, et al. *Arch Intern Med*. 2002 Jul 8;162(13):1515-20.
Quale JM, et al. *Clin Infect Dis*. 2002 Oct 1;35(7):834-41.
Tacconelli E, et al. *J Antimicrob Chemother*. 2008 Jan;61(1):26-38

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Longer Duration → Higher Risk of *C. diff*

CDI risk increases with duration

Table. Comparison of antibiotic days for case & noncase hospitalizations

	CDI positive n (%)	CDI negative n (%)	Adjusted hazard ratio (95% CI)
Antibiotic days, median (IQR)	14.0 (23)	7.0 (9)	
<4	22 (9)	2208 (22)	Ref
4 to 7	41 (17)	3701 (31)	1.4 (0.8, 2.4)
8 to 18	87 (36)	3097 (31)	3 (1.9, 5)
>18	91 (38)	1537 (16)	7.8 (4.6, 13.4)

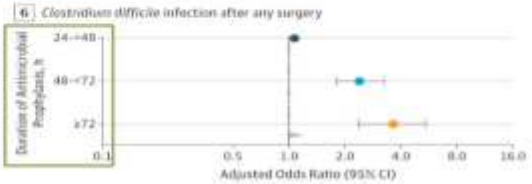

Figure. Adjusted odds of CDI by duration of antimicrobial prophylaxis

Slide courtesy of Cynthia Nguyen, PharmD, BCIDP, BCPS (AQ-ID)-presented at ID Week 2021

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Worst Offenders for *C. difficile*

Systematic Review and Meta-Analysis 2021

	OR	95% CI
Carbapenems	2.55	1.83, 3.55
3rd Generation Cephalosporins (Ceftriaxone)	2.13	1.63, 2.79
4th Generation Cephalosporins (Cefepime)	2.28	2.02, 2.56
Fluoroquinolones	1.34	1.13, 1.60
2nd Generation Cephalosporins	1.58	1.08, 2.30

These look familiar…

Slimings C, Riley TV. JAC. 2021;76:1676-88

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Worst Offenders for Resistance

	VRE	MRSA	ESBLs	CRE
2nd & 3rd Generation Cephalosporins				
Fluoroquinolones				
Carbapenems				

*OR = Odds ratio, RR = Risk Ratio
Extended spectrum beta-lactam

Same Antibiotics→More Resistance and *C. difficile*

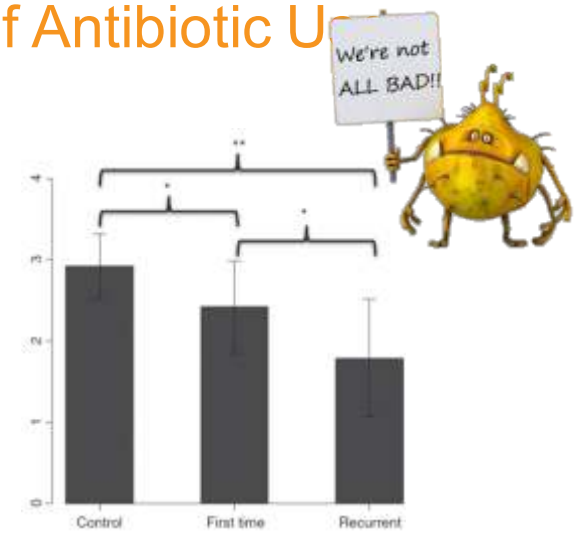
Bad news: Use these at your own risk

Good news: Avoid these and reduce risk of resistance *AND C. difficile*

Ostrowsky BE, et al. *Arch Intern Med*. 1999 Jul12;159(13):1467-72.
Quale JM, et al. *Clin Infect Dis*. 2002 Oct 1;35(7):834-41.
Carmeli Y, et al. *Emerg Infect Dis*. 2002 Aug;8(8):802-7.
Tacconelli E, et al. *J Antimicrob Chemother*. 2008 Jan;61(1):26-38.

Other Consequences of Antibiotic U

- Impact on microbiome
- Diversity of gut microbiome decreases with CDI and recurrent CDI



http://allergiesandyourgut.com/wp-content/uploads/2014/06/only-10-percent-human.jpg

Pharmacol Ther. 2016;43:1142-53.
Seekatz AM, et al. Antimicrob Agents Chemother. 2014;5(3)1-9.

Prescribing trends in Nigeria..

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What can we do to STOP it?

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Questions/Comments ?

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SPEAKER'S PROFILE

PROF. OYINLOLA ODUYEBO, FAMEDS

Professor of Clinical Microbiology

MB, BS (1986), M.Sc. Medical Microbiology (1995), FWACP (Lab med, 1998), FMCPath (1998), MD (2021), FRCPath 2023

A lecturer in the College of Medicine of the University of Lagos since 1998, teaching Medical Microbiology to medical students, postgraduate students, nurses and midwives. Also a Honorary consultant to the Lagos University Teaching Hospital, helping to manage the hospital laboratory, investigating and managing healthcare associated infections and training resident doctors.

Research interests have been around antibiotic stewardship, antimicrobial resistance and healthcare associated infections. The results of her research have helped to educate healthcare workers on rational antibiotic use and importance of adequate infection control practices. Currently, chairman of the antimicrobial stewardship program and also of the infection control program of the Lagos University Teaching Hospital. A member of the AMR technical working group in Nigeria. In collaboration with the British Society for Antimicrobial Chemotherapy and the Infection Control Africa Network, she led the development of the a 3-week Future learn MOOC training "antimicrobial stewardship for Africa".She is the National coordinator of the National Antimicrobial stewardship working group in Nigeria, an arm of the Clinical Microbiology and Infectious Diseases Society of Nigeria (CLIMIDSON).

SPEAKER'S PROFILE

DR. FOLAKE KOFO-IDOWU

Infectious Diseases Consultant

Dr. Folake Kofo-Idowu is an infectious diseases consultant, Double Board certified by the American Board of Internal medicine and medical specialties . She began her career with a medical education from Lagos State University before proceeding to complete a residency in internal medicine at the University of Maryland. Dr. Kofo-Idowu furthered to obtain a fellowship in infectious disease from the Medical College of Georgia and additional Masters of Public Health from the University of California, Berkeley. She has over 15 years of clinical medicine experience from both Nigeria and the United States. Previously, Dr. Folake worked as Assistant Professor at Medical College of Georgia and at the NIAID as a Medical Officer in the Division of AIDS (DAIDS), managing groundbreaking HIV and hepatitis research.

Presently, she works as a locums physician serving multiple health systems across the US, She is the CEO of IYEWO, a Primary Care start up in Lagos, and concurrently the Executive Director for Amal Outreach an non profit that facilitates access to healthcare and underserved community development. She is passionate about expanding health access and coverage as well as localizing global advancements for local development.

TOPIC: "Navigating Multidrug-Resistant (MDR) Infections: From Antibiotic Stewardship to Innovative Therapies"

SPEAKER'S PROFILE

DR. BABASEYI OYESOLA

BSc. MB. BS, FRCAI

Dr. Babaseyi Oyesola BSc. MB. BS, FRCAI, is an accomplished anesthetist and medial practitioner with over 25 years on the cutting edge of practicing medicine in anesthesiology and critical care. Doctor Oyesola is not only one of the Nigeria's foremost authorities on anesthesiology and intensive care, he is also a successful serial entrepreneur and passionate humanitarian who cares about the well-being of his fellow citizens.

He began his medical career after graduating with honors from the College of Medicine (CMUL), University of Lagos in Nigeria and he quickly rose through the ranks to lead a team of young doctors in anesthesiology at the University of Lagos.

Throughout his medical career Dr. Oyesola has made it a point to continue learning new techniques and procedures and improving his interpersonal leadership and teaching skills. He has already co-authored or published 8 important articles on medicine and at one point, took a year off his practice to join the University of Los Angeles in California as a visiting Assistant Professor in 1998.

After his successful one year US tenure, he returned to the UK when he became one of the lead consulting attending physicians at Medway Hospital in Gillingham in Kent, where he practiced for over 15 years. While in England, Dr. Oyesola partnered with a British medical technologist to develop the world's first unique portable operating room equipment and inventory device, based on his experience living and working in Nigeria. It is retailed as "OR in a BOX"

In 2008 Dr. Oyesola took a hiatus from his UK practice to return to Nigeria as the Chief Medical Director at Delta State University Teaching Hospital in Warri. He specifically oversaw the setup and training of young doctors and nurses to ensure that international medical standards and practices were formally introduced into the university hospital teaching system.

It was the time spent in Delta State that convinced Dr Oyesola to make the formal transition to Nigeria to give back to the country in the form of delivering advanced intensive medical care to its citizens at affordable rates.

Today, Dr. Oyesola has a successful medical devices company and is actively leading the setup of a Cardiac Intervention scheme in Nigeria, as well as an Intensive Care Unit (ICU) service, support already establish medical facilitates across the country.

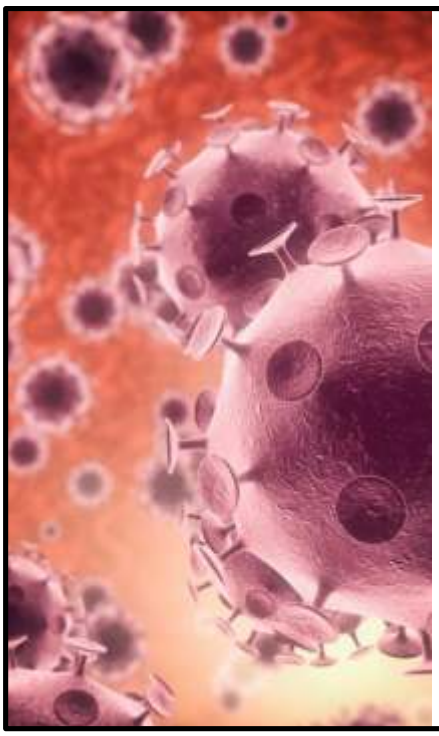
Antibiotic Resistance in Intensive Care Units in Nigeria: Challenges and Strategic Approaches

Addressing a Silent Crisis in Nigerian Healthcare

Presenter: Dr. Seyi Oyesola
Affiliation: Anesthesia and Critical Care Consultants (A3C)

Introduction to Antibiotic Resistance

- Antibiotic resistance is recognized as one of the biggest threats to global health.
- ICUs are high-risk environments due to critical patient profiles and heavy antibiotic usage.
- Overuse and misuse of antibiotics are driving resistance.
- ICUs globally are facing the consequences: higher mortality, longer hospital stays, and increased costs.
- Nigeria is no exception, with ICUs facing significant challenges.

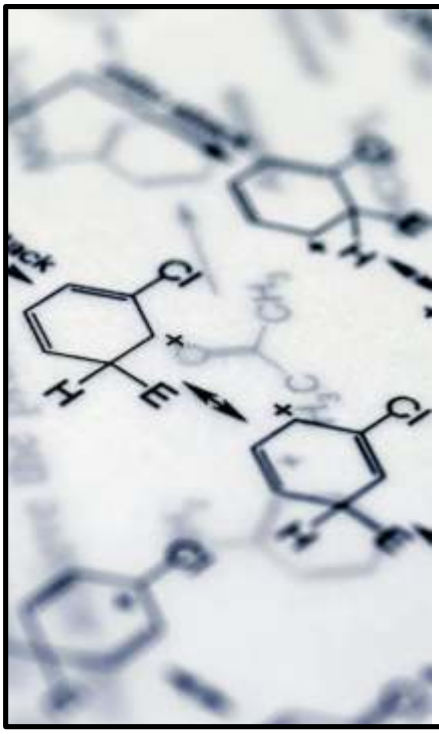


Global Overview of Antibiotic Resistance in ICUs

- Resistance rates are rising globally, particularly in resource-limited settings.
- High resistance rates are observed in pathogens like Staphylococcus aureus, Pseudomonas aeruginosa, and Klebsiella pneumoniae.
- 700,000 deaths annually worldwide due to resistant infections.
- By 2050, it is estimated that antibiotic resistance could cause 10 million deaths per year.

Epidemiology of Antibiotic Resistance in Nigerian ICUs

- Recent studies indicate alarming rates of resistance in Nigerian ICUs.
- Common pathogens like E. coli, Klebsiella pneumoniae, and Acinetobacter baumannii show high levels of resistance.
- Over 60% of ICU infections involve multidrug-resistant organisms.
- High resistance to first-line antibiotics, including ceftriaxone and amoxicillin-clavulanate.



Common Resistant Pathogens in Nigerian ICUs

- ICU patients are vulnerable to infections from pathogens like MRSA (Methicillin-Resistant Staphylococcus aureus) and ESBL (Extended-Spectrum Beta-Lactamase) producing bacteria.
- Common pathogens include MRSA, ESBL-producing Enterobacteriaceae, and carbapenem-resistant Acinetobacter baumannii.
- High prevalence of resistant Klebsiella pneumoniae and Pseudomonas aeruginosa.

Contributing Factors in Nigerian ICUs: Empirical Antibiotic Therapies

- Empirical antibiotic therapy is often necessary in ICUs, but without proper diagnostics, it leads to misuse.
- Delayed targeted treatment due to lack of rapid diagnostics exacerbates resistance.
- Over-reliance on broad-spectrum antibiotics.
- Delays in pathogen identification and susceptibility testing.
- Absence of local antibiograms guiding therapy decisions.

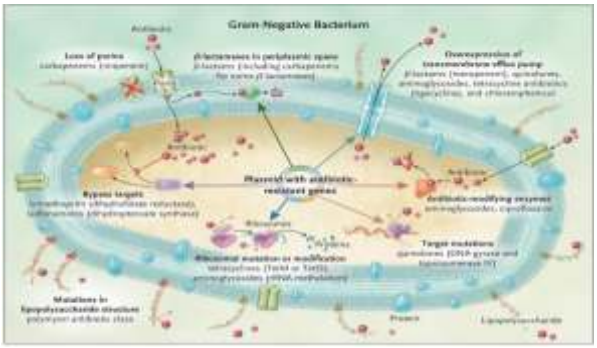
SPEAKER'S PROFILE

DR. DEANNE TABB

Pharm.D., MT (ASCP)
Infectious Disease Specialist Division of Pharmacy

Dr. Deanne Tabb received a BS in Medical Technology from Columbus State University and practiced in the area of Clinical Microbiology prior to earning her PharmD from Auburn University. She completed a Pharmacy Practice Residency at Columbus Regional Health Care System and an Infectious Disease Specialty at the Mayo Clinic in Rochester, Minnesota.

Dr. Tabb currently heads an Infectious Disease Pharmacy Service at Piedmont Columbus Midtown in Columbus, Georgia.



MDR GRAM NEGATIVE ORGANISMS: THE IMPACT OF CLINICAL MICROBIOLOGY ON ANTIBIOTIC SELECTION

Deanne Tabb PharmD, MT (ASCP)
Infectious Diseases Pharmacist

Objectives

- Demonstrate the clinical impact of select microbiology tests for GNR infections
- Highlight microbiology workflow
- Introduce microbiology regulatory requirement documentation for panels
- Review antimicrobial agents with spectrum for MDR gram negative bacteria

Case 1

CC: 73 y/o male found unresponsive, admitted for sepsis and neutropenia

PMH: esophageal cancer with port for active chemo, HTN, atrial fibrillation and diabetes

Treatment: initiated on empiric cefepime and vancomycin

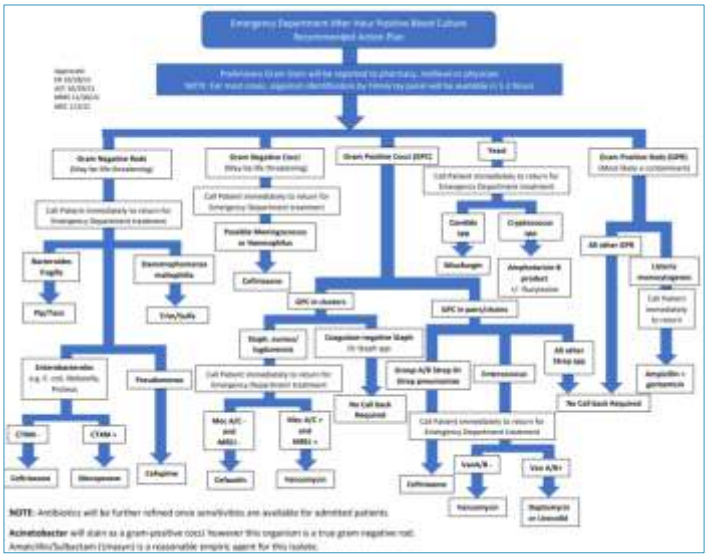
- Blood Culture (BC): GNR 4/4 bottles
- Two organisms identified
- Cefepime changed to Meropenem

Positive BC workflow

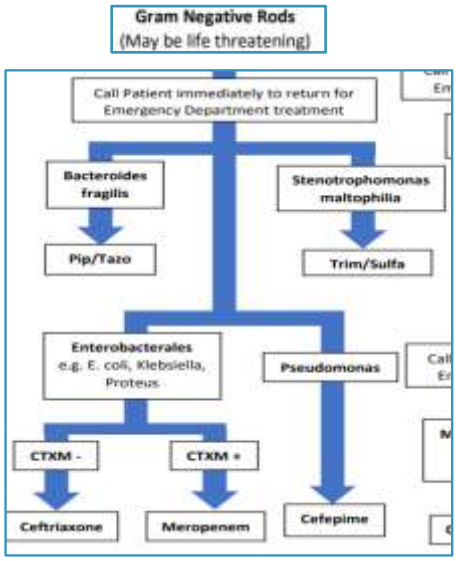
1. BACT Alert
2. Gram stain/plate/panic value called to patient location
3. If GNR or GPC, BCID Biofire FilmArray
4. No BCID if GPR

FilmArray Results drop in EPIC Best Practice Bucket

Positive Blood Culture Action



Positive Blood Culture Action



Susceptibilities

Adult blood cultures drawn from 2 different peripheral sites [1048887380] (Abnormal)

Lab Status: Preliminary result

Specimen: Blood, Venous

Blood Culture Result — Abnormal Stain !

Klebsiella varicola ?

Gram Stain Result — Gram negative bacili. !

Comment: ISOLATED FROM THE AEROBIC BOTTLE OF THE FIRST SET

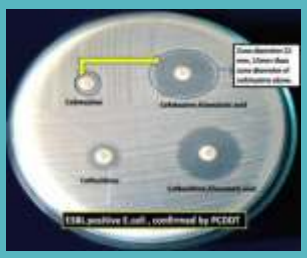
Narrative:

Abnormal Gram Stain for Blood Culture

Susceptibility

	Klebsiella varicola Not Specified (Preliminary)	
Amoxicillin + Clavulanate	<=8/4	Susceptible
Ampicillin	16	Intermediate
Ampicillin + Sulbactam	<=4/2	Susceptible
Aztreonam	<=4	Susceptible
Cefazolin	<=2	Susceptible
Cefepime	<=2	Susceptible
Cefoxitin	<=8	Susceptible
Ceftazidime	<=1	Susceptible
Ceftriaxone	<=1	Susceptible
Cefuroxime	<=4	Susceptible
Ciprofloxacin	<=0.25	Susceptible
Ertapenem	<=0.5	Susceptible
Gentamicin	<=2	Susceptible
Imipenem	<=1	Susceptible
Levofloxacin	<=0.5	Susceptible
Meropenem	<=1	Susceptible
Piperacillin + Tazobactam	<=8	Susceptible
Tetracycline	<=4	Susceptible
Tobramycin	<=2	Susceptible
Trimethoprim + Sulfamethoxazole	<=0.5/9.5	Susceptible

ESBL Epidemiology



Journal of clinical microbiology. 2021;59(6).

- CTX-M enzymes are the most common ESBLs in the United States
- TEM & SHV are also present
- A 2021 study detected ESBL genes in (13.3%) *Escherichia coli,* N = 2059, and (11.8%) of *Klebsiella pneumoniae,* N = 836)
  - Of these:
    - 92.5% carried CTX-M-encoding genes
    - 8.6% carried SHV-encoding genes
    - 1.2% carried TEM-encoding genes
- Prevalence can vary geographically: 5% Michigan - 26% Washington, DC

Lower Cephalosporin Breakpoints

A 2001 study examined the outcome of serious ESBL infections in patients treated with cephalosporins in which the organism was "susceptible" or intermediate" *in vitro*

- 54% of patients experienced clinical failure
- Statistically significant increase in failure when MICs rose closer to 8 (p = 0.004)

	MIC breakpoint for isolates in indicated category by:					
	CLSI M100-S19 (2009)			CLSI M100-S20 (2010)		
Agent	Susc	Int	Res	Sus	Int	Res
Cefazolin	≤8	16	≥32	≤1	2	≥4
Cefotaxime	≤8	16–32	≥64	≤1	2	≥4
Ceftriaxone	≤8	16–32	≥64	≤1	2	≥4
Ceftazidime	≤8	16	≥32	≤4	8	≥16
Aztreonam	≤8	16	≥32	≤4	8	≥16

	MIC breakpoint for isolates in indicated category by:					
	CLSI M100-S23 (2013)			CLSI M100-S24 (2014)		
Agent	Susc	Int	Res	Susc	SDD	Res
Cefepime	≤8	16	≥32	≤2	4–8	≥16

J Clin Microbiol. 2016;54(4):840-844.

Lower Cephalosporin Breakpoints

- A 2011 study aimed to determine how many ESBL-producing strains of *Klebsiella pneumoniae*, *E. coli*, and *Proteus mirabilis* test susceptible using the new recommended CLSI breakpoints
  - **All** 382 strains tested **resistant** to cefazolin, cefotaxime, and **ceftriaxone**
  - 85% - 96.7% of *P. mirabilis* strains tested susceptible to ceftazidime, cefepime, and aztreonam
  - 41.8% - 45.6% of *E. coli* strains tested susceptible to ceftazidime and cefepime
  - 20.1% of *K. pneumoniae* were susceptible to cefepime
- A 2017 narrative review of cefepime effectiveness in treating ESBL infections calls into question the use of cefepime

Table 3. Rate of Clinical Failure or Mortality With Cefepime Use for ESBL Infections.

MIC (μg/mL)	Kotapati et al[25] (N = 10)	LaBombardi et al[26] (N = 13)	Chopra et al[28] (N = 43)	Lee et al[27] (N = 17)	Paterson et al[12] (N = 3)	Bhat et al[30] (N = 11)	Wang et al[29] (N = 17)	Seo et al[31] (N = 6)	Total (N = 113)
≥8	3/4 (75%)	1/1 (100%)	11/26 (42%)	3/5 (60%)	–	1/4 (25%)	0/4 (0%)	–	19/44 (43.2%)
4	2/4 (50%)	–	1/4 (25%)	1/3 (33.3%)	–	2/3 (66.7%)	5/9 (55.5%)	–	11/23 (47.8%)
2	–	0/2 (0%)	5/13 (39%)	1/3 (33.3%)	1/2 (50%)	2/3 (66.7%)	–	3/4 (75%)	9/24 (37.5%)
≤1	1/2 (50%)	1/10 (10%)	–	1/6 (16.7%)	1/1 (100%)	–	2/4 (50%)	1/2 (50%)	7/25 (28.0%)

J Clin Microbiol. 2001;39(6):2206-2212.
J Clin Microbiol. 2011 Sep;49(9):3127-31.

Case # 2

CC: 75 y/o male presents to the ED for evaluation of abdominal pain and emesis

PMH: CHF, COPD, hypertension, hyperlipidemia

Diagnosed with sepsis from abdominal source

Treatment: initiated on empiric piperacillin/tazobactam

Blood Culture Identification 2 (BCID2) by PCR [1062420484] (Abnormal)
Lab Status: Final result — Specimen: Blood, Venous

Enterococcus faecalis	Not detected	Klebsiella oxytoca	Not detected
Enterococcus faecium	Not detected	Klebsiella pneumoniae group	Not detected
Listeria monocytogenes	Not detected	Proteus spp.	Not detected
Staphylococcus spp.	Not detected	Salmonella spp.	Not detected
Staphylococcus aureus	Not detected	Serratia marcescens	Not detected
Staphylococcus epidermidis	Not detected	Candida albicans	Not detected
Staphylococcus lugdunensis	Not detected	Candida auris	Not detected
Streptococcus spp.	Not detected	Candida glabrata	Not detected
Streptococcus agalactiae	Not detected	Candida krusei	Not detected
Streptococcus pneumoniae	Not detected	Candida parapsilosis	Not detected
Streptococcus pyogenes	Not detected	Candida tropicalis	Not detected
Acinetobacter calcoaceticus-baumannii complex	Not detected	Cryptococcus neoformans/gattii	Not detected
		CTX-M	Not detected
Bacteroides fragilis	Not detected	KPC	Not detected
Haemophilus influenzae	Not detected	mec A/C	N/A
Neisseria meningitidis	Not detected	NDM	Not detected
Pseudomonas aeruginosa	Not detected	van A/B	N/A
Stenotrophomonas maltophilia	Not detected	IMP	Not detected
Enterobacteriaceae	Detected !	mcr-1	Not detected
Enterobacter cloacae complex	Not detected	mecA/C and MREJ (MRSA)	N/A
Escherichia coli	Detected !	OXA-48-like	Not detected
Klebsiella aerogenes	Not detected	VIM	Not detected

Sensitivities

Adult blood cultures drawn from 2 different peripheral sites [1061997086] (Abnormal)
Lab Status: Preliminary result

Blood Culture Result — Specimen: Blood, Venous
Abnormal Stain !
Escherichia coli !

Comment:

Gram Stain Result — Gram negative bacilli. !

Comment: ISOLATED FROM THE ANAEROBIC BOTTLE OF THE FIRST SET

Treatment: zosyn switched to meropenem

Internal MicroScan Rule: piperacillin/tazobactam is suppressed for ESBL E coli from BC isolates unless resistant to zosyn

Abnormal Gram Stain for Blood Culture.

Susceptibility

	Escherichia coli Not Specified (Preliminary)	
Amoxicillin + Clavulanate	<=8/4	Susceptible
Ampicillin	>16	Resistant
Ampicillin + Sulbactam	>16/8	Resistant
Aztreonam	>16	Resistant
Cefazolin	>16	Resistant
Cefepime	>16	Resistant
Cefotaxime	>32	Resistant
Cefoxitin	<=8	Susceptible
Ceftazidime	>16	Resistant
Ceftazidime/Avibactam	<=4	Susceptible *
Ceftolozane/Tazobactam	<=2	Susceptible *
Ceftriaxone	>32	Resistant
Cefuroxime	>16	Resistant
Ciprofloxacin	>2	Resistant
Ertapenem	<=0.5	Susceptible
Gentamicin	<=2	Susceptible
Imipenem	<=1	Susceptible
Levofloxacin	>4	Resistant
Meropenem	<=1	Susceptible
Meropenem/Vaborbactam	<=2	Susceptible *
Tetracycline	<=4	Susceptible
Tobramycin	<=2	Susceptible
Trimethoprim + Sulfamethoxazole	>2/38	Resistant

MERINO Trial

Randomized non-inferiority international parallel trial: Ceftriaxone Resistant *E. coli/Klebsiella pneumoniae* Bloodstream infections

- **Interventions:** piperacillin-tazobactam 4.5 g every 6 hours vs meropenem 1 g every 8 hours
- Number of enrolled patients: 378
- **Primary Outcome:** all-cause mortality at 30 days
  - 12.3% vs 3.7% (risk difference, 8.6%); p = 0.90 for noninferiority
- **Secondary Outcome:** clinical and microbiological resolution by Day 4
  - 68.4% vs 74.6% (risk difference, -6.2%); p = 0.19
- The study was ***stopped early due to a 3-fold higher 30-day mortality*** in the piperacillin-tazobactam group
- Limitation: The presence of narrow-spectrum oxacillinases (blaOXA-1 and variants) was found in 67.6% of all strains and could have potentially compromised β-lactamase inhibition by tazobactam

MERINO-2 Trial

Randomized non-inferiority international parallel trial: AmpC β- Lactamase-Producing *Enterobacter* spp, *Citrobacter freundii, Morganella morganii, Providencia* spp, or *Serratia marcescens* Bloodstream Infections

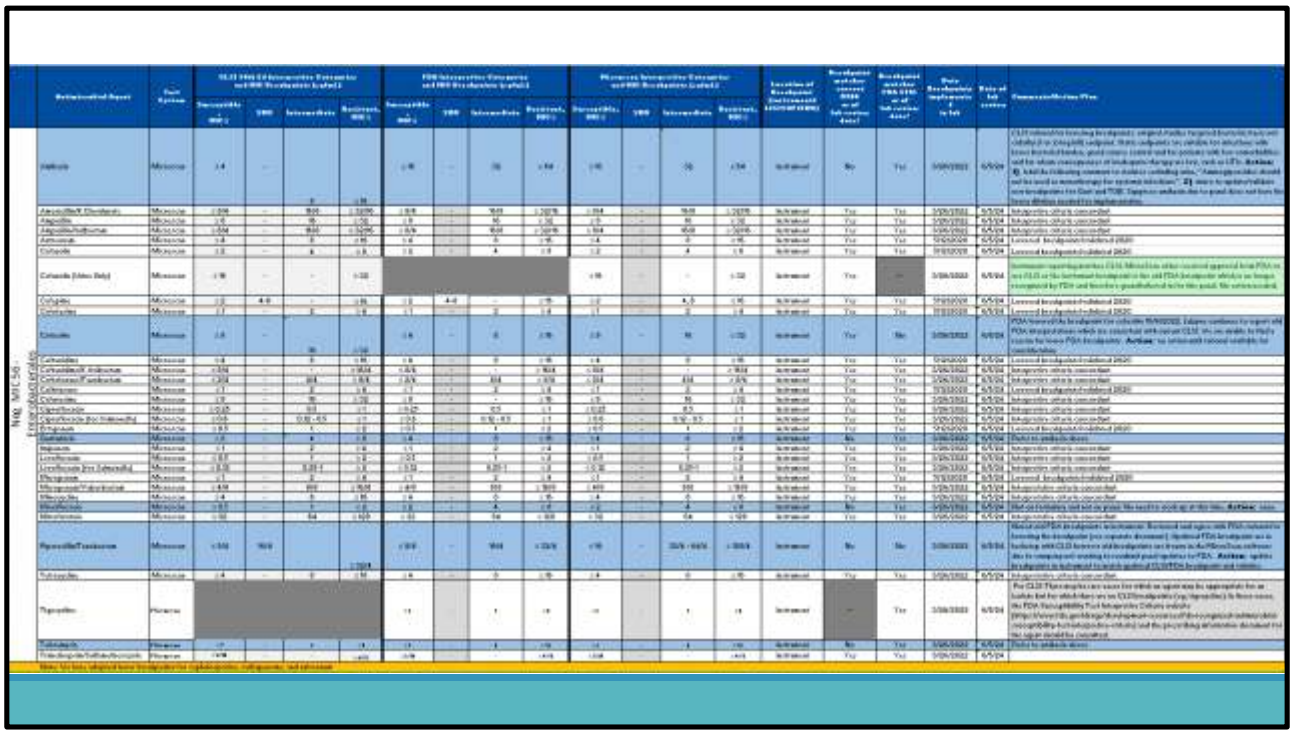
- **Interventions:** piperacillin-tazobactam 4.5 g every 6 hours vs meropenem 1g every 8 hours
- Number of enrolled patients: 72
- **Primary Outcome:** all-cause mortality at 30 days
  - 29% vs 21% (risk difference, 8%); p=0.41
- **Secondary Outcome:** clinical and microbiological resolution by Day 5
  - 74% vs 82% (risk difference, -9%)
- Study terminated due to slow accrual

JAMA. 2018;320(10):984-994.
Open Forum Infect Dis. 2021;8(8)

Enterobacterales (not including *Salmonella/Shigella*) 6.6.24

Tier 1 Agents that are appropriate for routine, primary testing and reporting	Tier 2 Appropriate for routine testing but may be reported following cascade rules established by the institution	Tier 3 Appropriate for routine, primary testing in institutions that serve patients at high risk for MDROs but should only be reported following cascade rules established by the institution	Tier 4 May warrant testing and reporting by clinician request if agents in other tiers are not optimal because of various factors	Unavailable
Ampicillin Ampicillin-sulbactam Amoxicillin-clavulanate Cefazolin Ceftriaxone Cefoxitin/cefotetan[10] Gentamicin Ciprofloxacin Levofloxacin Tetracycline Trimethoprim-sulfamethoxazole	Ertapenem, Imipenem, Meropenem[2] Tobramycin[3] Piperacillin-tazobactam[11] Cefepime[12] Aztreonam[5] Amikacin[11]	Ceftazidime-avibactam, meropenem-vaborbactam[4]	Cefiderocol[5] Ceftaroline[6] Ceftazidime[6] Ceftolozane-tazobactam[6] cefuroxime[9]	Plazomicin, imipenem-relebactam[7] Cefotaxime[8]
Urine only				
Nitrofurantoin				Fosfomycin[7] (*Escherichia coli*)

1. CLSI designates as tier 4 agent. Recommend designation as a tier 2 agent to be suppressed unless isolate intermediate or resistant to either Levaquin or ciprofloxacin. If released, add the following comment to micro report, "**Used for patients with severe Beta-lactam/Cephalosporin allergy**"
2. Recommend suppression unless cascade criteria are met or available upon request for beta-lactam allergic patients. Cascade criteria: report meropenem/ertapenem for Enterobacterales resistant to ceftriaxone – surrogate marker for ESBL
3. Recommend suppression unless resistant to gentamicin (cascade criteria would need to be built)
4. Recommend suppression unless the following **cascade criteria are met: isolate identified as a carbapenem resistant strain**
5. CLSI designates as tier 3 agent, recommend designation as tier 4 agent available upon request only (primarily used for multi-drug resistant Pseudomonas or Acinetobacter infections)
6. Available upon request
7. CLSI designates as tier 3 agents, however no in-vitro susceptibility methodology available at this time (imipenem-relebactam not included on MicroScan panel and we currently do not have any e-tests ordered)
8. CLSI designates as tier 1 agent, recommend always suppress, drug no longer available in the United States
9. Cefuroxime on the panel represents 2 grams IV Q8H only dosing. We have not ordered or used IV cefuroxime in many years. We primarily use oral cefuroxime for UTI infections which must be inferred from cefazolin. Recommend always suppress with results available upon request.
10. CLSI designates Cefotetan/Cefoxitin as tier 2. Recommend routinely reporting.
11. Zosyn is designated Tier 1. However, recommend Tier 2 with suppression unless urinary isolate is intermediate or resistant to ceftriaxone then report for urine source only. Always report if resistant.



Antibiotics for Extended-Spectrum-β-lactamase-producing (ESBL)

ESBLs inactivate penicillins, cephalosporins, and aztreonam

- Harbor additional genes that mediate resistance to other antibiotics
- Most prevalent in:
  - *Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, and *Proteus mirabilis*

Antibiotics for the Treatment of ESBL Infections in Adults	
Meropenem/Ertapenem/Imipenem	**Levofloxacin/Ciprofloxacin**
Ceftazidime-avibactam	**Trimethoprim-sulfamethoxazole**
Ceftolozane-tazobactam	**Cefiderocol**

Clinical Infectious Diseases. Published online July 18, 2023.

Case 3

CC: 79 y/o female day-25 hospitalization

PMH: HTN, hypothyroidism

Diagnosis: new severe sepsis with suspected sacral wound source initiated on empiric vancomycin and Meropenem due to recent Rocephin/Zosyn exposure

Changed to targeted Treatment: high dose Unasyn 9 gm infused over 4-hours IV Q8h and minocycline 200 mg IV Q12h

CRAB Sensitivities

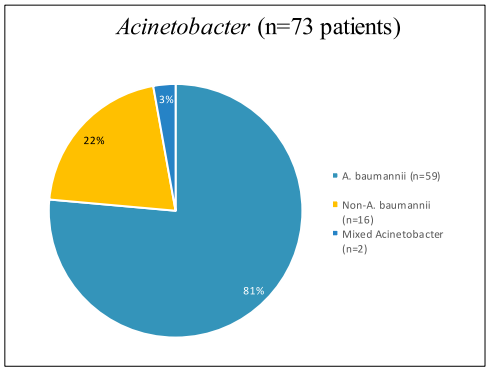
Infectious Diseases Society of America 2024 Guidance on the Treatment of Antimicrobial-Resistant Gram-Negative Infections

There is no clear antimicrobial "standard of care" regimen for carbapenem-resistant Acinetobacter to compare treatment options.

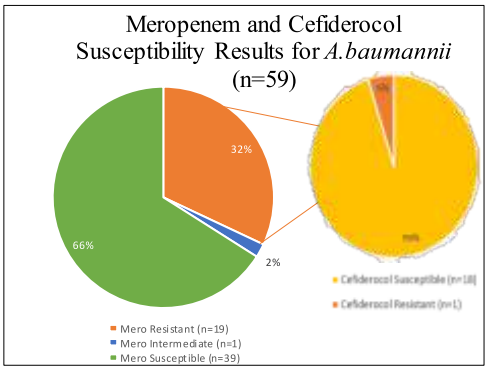
Preferred	Alternative *	Never Suggested
Sulbactam-durlobactam § + **Meropenem** or imipenem-cilastatin	**Ampicillin-sulbactam** § (high dose) + Cefiderocol ¶, **Minocycline** (high dose), Tigecycline (high dose) ¥, or Polymyxin B *Based on patient and infection specific factors*	Monotherapy Rifamycins (rifampin, rifabutin, rifapentine) Fosfomycin Nebulized antibiotics Omadacycline
Special Circumstances: • Colistin is favored over polymyxin B (in a combo regimen) for CRAB UTIs. It converts to its active form in the urinary tract while there is minimal polymyxin excretion in the urine • Eravacycline (in place of minocycline or tigecycline) use should be limited to situations when other agents are not active, available, or tolerated		
* When sulbactam-durlobactam is not available § Use of a regimen containing sulbactam is suggested for treatment of carbapenem-resistant CRAB infections. **For high dose amp/sulbactam, the concentration of sulbactam should achieve PK target for CRAB with sulbactam MICs up to 16-32 mcg/mL.** ¶ The IDSA panel suggests reserving cefiderocol until other regimens have been exhausted ¥ Minocycline is preferred over tigecycline		

Clin Infect Dis. 2024; ciae403:48-60

Internal data



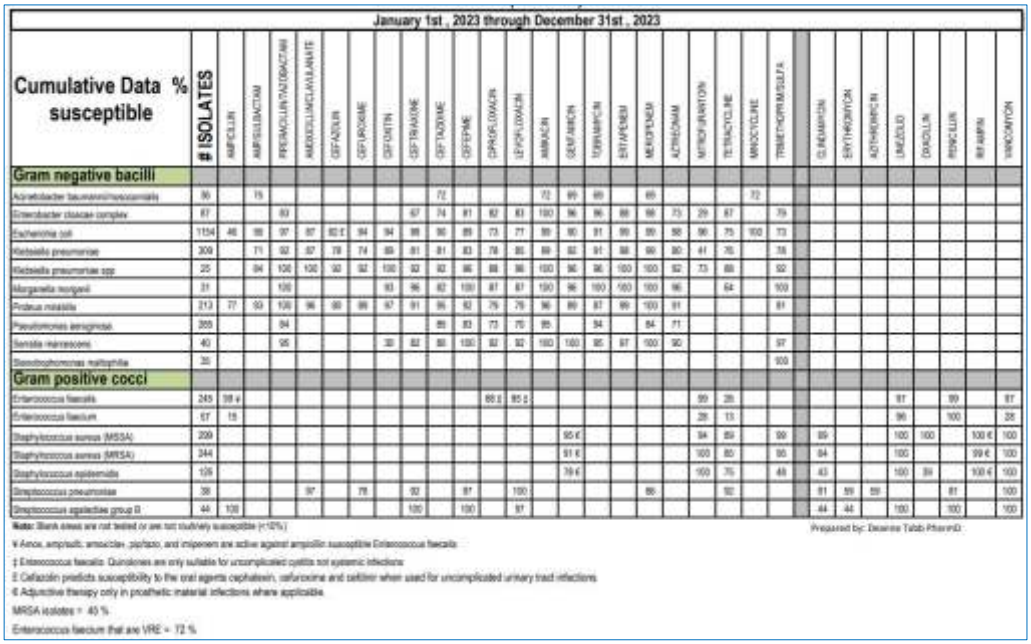
2 patients had both *A. baumannii* and a non-*A. baumannii* isolate (*A. radioresistens*)
1 patient had two different non-*A. baumannii* isolates (*A. pittii* and *A. lactucae*)



The **intermediate** isolate was <u>not</u> tested for susceptibility to cefiderocol
95% of carbapenem-resistant *A. baumannii* isolates were susceptible to cefiderocol

Susceptibilities for non-*A. baumannii* isolates (n=17)

- All isolates (n=17) were susceptible to Meropenem and Tetracycline (inference for minocycline)
- Susceptibility results on these isolates for Cefiderocol were not reported due to Meropenem sensitive, per cascade rule
- Susceptibility results for Cefepime not reported



January 1st , 2023 through December 31st , 2023

Cumulative Data % susceptible	# ISOLATES	AMPICILLIN	AMPICILLIN/SULBACTAM	PIPERACILLIN/TAZOBACTAM	AMOXICILLIN/CLAVULANATE	CEFAZOLIN	CEFUROXIME	CEFOXITIN	CEFTRIAXONE	CEFTAZIDIME	CEFEPIME	CIPROFLOXACIN	LEVOFLOXACIN	AMIKACIN	GENTAMICIN	TOBRAMYCIN	ERTAPENEM	MEROPENEM	AZTREONAM	MINOCYCLINE	TETRACYCLINE	MINOCYCLINE	TRIMETHOPRIM/SULFA	CLINDAMYCIN	ERYTHROMYCIN	AZITHROMYCIN	LINEZOLID	DOXYCYCLIN	PENICILLIN	RIFAMPIN	VANCOMYCIN
Gram negative bacilli																															
Acinetobacter baumannii/calcoaceticus	90		15							72				72	69	69		69				72									
Enterobacter cloacae complex	87			93					67	74	81	82	83	100	96	96	88	98	73	29	87		79								
Escherichia coli	1154	46	88	97	87	82 ‡	94	94	88	90	89	73	77	99	90	91	99	99	98	96	75	100	73								
Klebsiella pneumoniae	209		71	92	87	78	74	89	81	81	83	78	85	99	92	91	98	99	90	41	76		78								
Klebsiella pneumoniae spp	25		84	100	100	92	92	100	92	92	96	88	96	100	96	96	100	100	92	73	88		92								
Morganella morganii	31			100				93	96	82	100	87	87	100	96	100	100	100	96		64		100								
Proteus mirabilis	213	77	99	100	96	98	99	97	91	96	92	79	79	96	89	87	99	100	91				91								
Pseudomonas aeruginosa	355			84					99	93	73	70	95		94		94	71													
Serratia marcescens	40			95				30	82	88	100	82	92	100	100	95	97	100	90				97								
Stenotrophomonas maltophilia	35																						100								
Gram positive cocci																															
Enterococcus faecalis	245	98 ¥										86 ‡	85 ‡							99	28						97		99		97
Enterococcus faecium	67	15																		28	13						96		100		28
Staphylococcus aureus (MSSA)	209														90 €					94	89		99	89			100	100		100 €	100
Staphylococcus aureus (MRSA)	344														91 €					100	80		95	94			100			99 €	100
Staphylococcus epidermidis	126														78 €					100	75		48	43			100	89		100 €	100
Streptococcus pneumoniae	38				97		78		92		87		100					86			92			81	59	59			81		100
Streptococcus agalactiae group B	44	100							100		100		97											44	44		100		100		100

Note: Blank areas are not tested or are not routinely susceptible (>12%)

Prepared by: Deanne Tabb PharmD

¥ Amox, ampisulb, amoxicillin, piperacillin, and imipenem are active against ampicillin susceptible Enterococcus faecalis

‡ Enterococcus faecalis: Quinolones are only suitable for uncomplicated cystitis not systemic infections

Σ Cefazolin predicts susceptibility to the oral agents cephalexin, cefuroxime and cefdinir when used for uncomplicated urinary tract infections

€ Adjunctive therapy only in prosthetic material infections where applicable

MRSA isolates = 45 %

Enterococcus faecium that are VRE = 72 %

Current Reporting

	Acinetobacter
Amikacin	
Ampicillin + Sulbactam	
Aztreonam	
Cefepime (MIC only)	
Cefotaxime	
Ceftazidime	
Ceftriaxone	
Gentamicin	
Imipenem	
Meropenem	
Tetracycline	
Tobramycin	
Trimethoprim + Sulfamethoxazole	

Routine Reporting

	Acinetobacter
Ampicillin + Sulbactam	
Cefepime	
Gentamicin	
Tobramycin	
Ciprofloxacin[1]	
Levofloxacin[1]	

Conditional Reporting

	Acinetobacter
Meropenem, Imipenem[2]	
Amikacin[3]	
Minocycline[4]	
Ceftazidime[5]	
Cefiderocol[6]	
Doxycycline + Polymyxin B/E (not available on panel)	
Ceftriaxone[7]	
Tetracycline[7]	
Piperacillin-tazobactam[7]	
Tigecycline[8]	
Trimethoprim + Sulfamethoxazole[9]	

1. No FDA breakpoints available with the updated MicroScan software, version (labPro 5.0). If the sensitivities and interpretations do not cross the interface, manually report the MIC values without interpretations.
2. CLSI designates as tier 2, recommend cascade, report if resistant to cefepime or ceftazidime
3. CLSI designates as tier 2, recommend cascade, report if resistant to tobramycin and gentamicin
4. CLSI designates as tier 2, recommend cascade, report if resistant to meropenem
5. CLSI designates as tier 1, Recommend designation as a tier 2 due to nonformulary status. An additional cascade would include only report if isolate resistant to cefepime but sensitive to ceftazidime
6. CLSI designates as tier 3, recommend cascade, set up Kirby-Bauer and report if resistant to meropenem
7. Suppress, available by physician request only. Questionable clinical utility. Note: zosyn does not cross the interface.
8. Not included in CLSI, recommend cascade, report MIC if resistant to meropenem. Some providers are using this value for Eravacycline inference.
9. Suppress. However, needs to be available for ID view. May be of clinical use in special complicated ID situations.

Finalized 6.6.24

Sulbactam-durlobactam (Xacduro)

- **Dosing**: sulbactam 1 g/durlobactam 1 g every 6 hours, infused over 3 hours
- **Spectrum**: *Acinetobacter baumannii-calcoaceticus* complex
- **FDA Indications**
  - Hospital-acquired pneumonia and ventilator-associated pneumonia, caused by susceptible isolates of *Acinetobacter baumannii-calcoaceticus* complex

ATTACK Trial for HABP/VABP Infections			
	Sulbactam-durlobactam	**Colistin**	
28-day all-cause mortality	12/63 (19%)	20/62 (32%)	Difference: -13.2% (95 CI, -30.0 to 3.5)
Likelihood of clinical cure	62%	40%	p = 0.016
Nephrotoxicity	12/91 (13%)	32/85 (38%)	p < 0.001

Lancet Infect Dis. 2023;23(9):1072-1084.
Xacduro (sulbactam-durlobactam) [package insert]. 2023.

Cefiderocol (Fetroja)

Spectrum: *Acinetobacter baumannii* complex, *Enterobacter cloacae* complex, *Pseudomonas, Klebsiella, Serratia, E. coli, Proteus*

- **FDA Indications**:
  - Complicated urinary tract infections, including pyelonephritis
  - Hospital-acquired pneumonia and ventilator-associated pneumonia
- **Dosing**: 2 grams IV every 8 hours, infused over 3 hours

Fetroja (Cefiderocol) [package insert]. 2019.
J Clin Med. 2021 Mar 4;10(5):1068.
Lancet. Infect. Dis. 2021;21:213–225.

Reduced Susceptibility to Cefiderocol

Reduced Susceptibility to Cefiderocol MICs of ≥ 1 mg/mL What Antibiotic to Use Now?												
% Susceptibility	**# Isolates**	**Cefepime/zidebactam**	**Cefiderocol/avibactam**	**Cefiderocol/nacubactam**	**Cefiderocol/relebactam**	**Cefiderocol/taniborbactam**	**Cefiderocol/vaborbactam**	**Cefiderocol/zidebactam**	**Imipenem/relebactm**	**Meropenem/nacubactam**	**Meropenem/vaborbactam**	**Sulbactam/durlobactam**
Acinetobacter baumannii	**11**	--	>90	--	>90	>90	--	>90	--	--	--	72.7
Enterobacterales	**67**	91	64.7	74.6	59.7	76.1	22.4	91	--	71	--	--
Pseudomonas aeruginosa	**9**	--	≤44.4	≤44.4	≤44.4	≤44.4	22.2	55.6	55.6	--	55.6	--

Deresinski SC, ed. In the Literature. Clinical Infectious Diseases. 2024;78(3):i-iv.

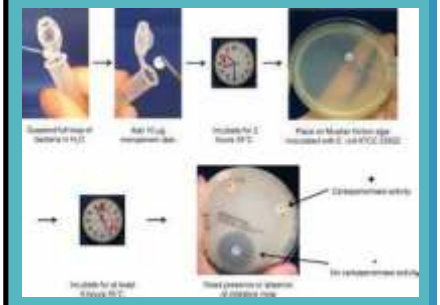
Antibiotics for KPC

- Carbapenemases are β-lactamases that have the ability to hydrolyze penicillin's, cephalosporins, monobactams, and carbapenems
- *Klebsiella pneumoniae* carbapenemases (KPC) are the most common carbapenemases within the U.S
- Other organisms that are potential KPC-producers include the following:
  - *Pseudomonas aeruginosa, Escherichia coli, Klebsiella oxytoca, Enterobacter spp.,* and *Citrobacter freundii*

Antibiotics for the Treatment of KPC
Ceftazidime-avibactam
Meropenem-vaborbactam
Imipenem-cilastatin-relebactam
Alternative Treatment
Cefiderocol
Tigecycline (Excluding bloodstream or urine)
Eravacycline (Excluding bloodstream or urine)

Clinical Infectious Diseases. Published online July 18, 2023.

Testing for Resistance
(modified CIM/Carba-R)



I. KPC
II. NDM
III. VIM
IV. IMP
V. OXA-48

Ceftazidime-avibactam (Avycaz)

Spectrum: Streptococci, MDR Enterobacterales (ESBL and KPC), Pseudomonas

- **FDA Indications**
  - Complicated intra-abdominal infections, in combination with metronidazole
  - Complicated urinary tract infections
  - Hospital-acquired pneumonia and ventilator-associated pneumonia
- **Dosing**: 2.5 g (ceftazidime 2 g and avibactam 0.5g) every 8 hours, over 2 hours

Table 23. 28-Day All-cause Mortality and Clinical Cure Rates from the Phase 3 HABP/VABP Trial, ITT and micro-ITT Populations

Study Endpoint (Population)	*AVYCAZ[a] n/N (%)*	*Meropenem[b] n/N (%)*	*Treatment Difference (95% CI)[c]*
28-Day all-cause mortality (ITT)	42/436 (9.6)	36/434 (8.3)	1.5 (- 2.4, 5.3)[c]
micro-ITT	22/187 (11.8)	19/195 (9.7)	2.1 (- 4.1, 8.4)[c]
Clinical cure (ITT)	293/436 (67.2)	300/434 (69.1)	- 1.9 (- 8.1, 4.3)[d,e]

[a] AVYCAZ 2.5 grams (ceftazidime 2 grams and avibactam 0.5 grams) IV every 8 hours
[b] 1 gram IV every 8 hours
[c] The 95% confidence interval (CI) was calculated based on Greenwood's variance estimates.
[d] A quantitative estimate of treatment effect has not been established for the clinical cure endpoint.
[e] The 95% confidence interval (CI) was calculated using an unstratified Miettinen and Nurminen method.

Antimicrob Agents Chemother. 2018;62(11):e02590-17.
Open Forum Infect Dis. 2019;6(4):ofz149.
Avycaz (ceftazidime-avybactam) [package insert]. 2024.

Meropenem-vaborbactam (Vabomere)

Spectrum: Enterobacterales (ESBL and KPC), Pseudomonas, MSSA, Streptococcus, anaerobes

- **FDA Indications**
  - Complicated urinary tract infections
- **Off Label:** limited randomized open label and observational studies
  - Carbapenem-resistant Enterobacterales in hospital-acquired or ventilator-associated pneumonia, bloodstream infection, or complicated intra-abdominal infection
  - **Dosing**: 4 g (meropenem 2 g and vaborbactam 2 g) every 8 hours, infused over 3 hours

JAMA. 2018;319(8):788-799.
Vabomere (meropenem-vaborbactam) [package insert]. 2023.

Imipenem-relebactam (Recarbrio)

- **Spectrum**: E. faecalis, MSSA, Streptococci, Norcadia, Enterobacterales (ESBL and KPC), Pseudomonas, non-Enterobacterales, anaerobes
- **FDA Indications**
  - Complicated intra-abdominal infections
  - Complicated urinary tract infections
  - Hospital-acquired pneumonia and ventilator-associated pneumonia

Dosing: 1.25 g (imipenem 500 mg, cilastatin 500 mg, and relebactam 250 mg) every 6 hours, infused over 30 minutes

Table 7: Day 28 All-Cause Mortality and Clinical Response Rates at EFU from Trial 1 of Hospital-acquired Bacterial Pneumonia and Ventilator-associated Bacterial Pneumonia (HABP/VABP) (MITT Population)

	RECARBRIO		Piperacillin/Tazobactam		Treatment Difference	
	n/m	(%)	n/m	(%)	%[a]	(95% CI)[a]
All-Cause Mortality Through Day 28[b,c]	**42/264**	**(15.9)**	**57/267**	**(21.3)**	**-5.3**	**(-11.9, 1.2)**
Non-ventilated HABP	18/142	(12.7)	15/131	(11.5)	1.2	(-6.8, 9.1)
Ventilated HABP/VABP	24/122	(19.7)	42/136	(30.9)	-11.2	(-21.6, -0.5)
Clinical Response at EFU[c]	**161/264**	**(61.0)**	**149/267**	**(55.8)**	**5.0**	**(-3.2, 13.2)**
Non-ventilated HABP	95/142	(66.9)	87/131	(66.4)	0.5	(-10.7, 11.7)
Ventilated HABP/VABP	66/122	(54.1)	62/136	(45.6)	8.5	(-3.7, 20.5)

[a]Treatment differences and 95% confidence intervals are based on Miettinen & Nurminen method.
[b]n/m = number of subjects with survival status of death or unknown / number of modified intent-to-treat subjects.
[c]n/m = number of subjects with a favorable clinical response / number of modified intent-to-treat subjects.
[d]One subject in the RECARBRIO arm had unknown mortality status at Day 28 which was counted as a death.
EFU = early follow up

Clin Infect Dis. 2021;73(11):e4539-e4548.
Recarbrio (imipenem, cilastatin, and relebactam) [package insert]. 2023

Antibiotics for New Delhi Metallo-β-lactamase

- NDM enzymes are capable of conferring resistance to almost all β-lactam antimicrobial drugs including carbapenems. Class B NDM contain zinc in the active site. (*Klebsiella pneumoniae* or *Escherichia coli)*
- NDM encoding genes are highly transmittable, located on plasmids, outbreaks reported[2]
- 32 NDM variants have been identified
  - NDM-1, NDM-4, NDM-5, and NDM-7 variants remain dominant globally with some exhibiting increased carbapenemase activity compared with NDM-1
  - All US isolates studied harbored bla_{NDM}

Antibiotics for the Treatment of NDM Beta Lactamase Enterobacterales Infections in Adults
Ceftazidime-avibactam + aztreonam Cefiderocol (Breakpoint < = 4mg/L) Tigecycline > Eravacycline
Polymyxins 30-80% (*intrinsically resistant organisms: Proteus, Morganella, Providencia and Serratia spp)

Clinical Infectious Diseases. Published online July 18, 2023
Treatment of Severe Infections Due to Metallo-Betalactamases Enterobacterales in Critically Ill Patients. 2022;11(2):144-144.
Emerging Infectious Diseases. 2021;27(10):2628-2637.
Antimicrobial Agents and Chemotherapy. 2020;64(9).
Clinical Microbiology Reviews. 2007;20(3):440-458.

Aztreonam-avibactam (Emblaveo)

- Loading Dose: aztreonam 2 g and avibactam 0.67 g
  - Maintenance Dose: aztreonam 1.5 g and avibactam 0.5 g
- Spectrum: metallo-beta-lactamases-producing Enterobacterales and Pseudomonas
- Study Indications
  - Complicated intra-abdominal infections with flagyl
  - Complicated urinary tract infections
  - Hospital-acquired pneumonia and ventilator-associated pneumonia (REVISIT Trial)

	HAP/VAP	
ITT Analysis Set	**ATM-AVI (n = 74)**	**MER ± COL (n = 36)**
Cure, n (%) [95% CI]	34 (45.9) [34.9, 57.3]	15 (41.7) [26.7, 57.9]
Difference, % (95% CI)	4.3 (-25.6, 32.2)	
CE Analysis Set	**ATM-AVI (n = 45)**	**MER ± COL (n = 22)**
Cure, n (%) [95% CI]	21 (46.7) [32.7, 61.1]	12 (54.5) [34.3, 73.7]
Difference, % (95% CI)	-7.9 (-42.8; 29.4)	

Open Forum Infect Dis. 2023;10(Suppl 2):ofad500.2476.

Antibiotics for OXA-48-like-producer

- OXA-48 is a carbapenem-hydrolyzing class D ß-lactamase
  - OXA-48 is not inhibited by clavulanic acid, tazobactam, sulbactam, or carbapenems
  - Most do not hydrolyze third and fourth generation cephalosporins
  - Producers lacking ESBLs remain susceptible to these agents
  - Most commonly in *Escherichia coli and Klebsiella Pneumoniae*

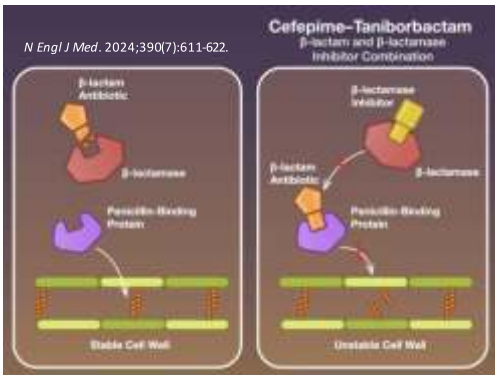
Antibiotics for the Treatment of OXA-48-like-producer Infections in Adults	
Ceftazidime-avibactam	**Tigecycline**[1]
Cefiderocol	**Eravacycline**[1]

1. Not to be used in bacteremia or urinary tract infections

Clinical Infectious Diseases. Published online July 18, 2023.
Antimicrob Agents Chemother. 2022 Aug 16;66(8):e0021622.
Journal of Antimicrobial Chemotherapy, Volume 67, Issue 7, July 2012, Pages 1597–1606

Cefepime-taniborbactam

- **Dosing**: 2.5 g (cefepime 2 g and taniborbactam 0.5 g) every 8 hours, infused over 2 hours
- **Spectrum**: carbapenem resistant *Enterobacterales*, carbapenem resistant *Pseudomonas*
- **Study Indications**
  - Complicated urinary tract infections
  - Hospital-acquired pneumonia and ventilator-associated pneumonia (CERTAIN-2 study will begin October 2024)

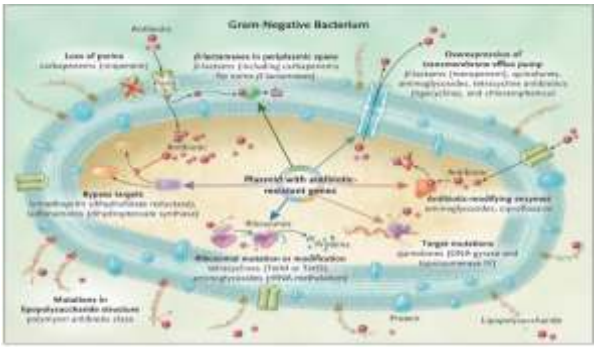


N Engl J Med. 2024;390(7):611-622.

Agent	KPC-producer	NDM-producer	OXA-48-like-producer	Carbapenem-resistant *Pseudomonas aeruginosa*	Carbapenem-resistant *Acinetobacter baumannii*	*Stenotrophomonas maltophilia*
Aztreonam-avibactam						
Cefiderocol						
Ceftazidime-avibactam[1]						
Ceftolozane-tazobactam[1]						
Eravacycline[1,2]						
Fosfomycin (intravenous)						
Imipenem-relebactam[3]						
Meropenem-vaborbactam[1]						
Plazomicin[1,4]						
Polymyxin B[1,5] or Colistin[1,5]						
Tigecycline[1,2]						

Figure 1. Select antibiotics with activity against carbapenem-resistant organisms. Green, susceptibility anticipated to be >80%; yellow, susceptibility anticipated to be 30% to 80%; red, intrinsic resistance or susceptibility anticipated to be <30%. [1], US Food and Drug Administration–approved agent; [2], synthetic tetracycline derivative; [3], imipenem-cilastatin–relebactam; [4], synthetic aminoglycoside; [5], polymyxin class. Abbreviations: KPC, *Klebsiella pneumoniae* carbapenemase; NDM, New Delhi metallo-β-lactamase.

Clinical Journal of the Pediatric Infectious Diseases Society. 2019;8(3):251-260.



MDR GRAM NEGATIVE ORGANISMS: THE IMPACT OF CLINICAL MICROBIOLOGY ON ANTIBIOTIC SELECTION

Deanne Tabb PharmD, MT (ASCP)
Infectious Diseases Pharmacist

SPEAKER'S PROFILE

MOBOLAJI OGUNSAKIN

MD MPH MBA FACP

Mobolaji Ogunsakin MD MPH MBA FACP I am a fellowship trained and board certified infectious disease attending physician for the last twenty seven years. I had my medical school training at the Obafemi Awolowo University (then University of Ife), Faculty of Health Sciences and Medical School in Ile-Ife, Nigeria. I graduated from Medical school in 1982. I did my internal medicine residency and infectious disease fellowship training at the Nassau University Medical center in East Meadow, New York.

I completed a two year Executive Masters in Business Administration (EMBA) program at the Wesleyan College in Macon, Georgia in June 2012. My focus was on the effect of globalization on the emergence and spread of communicable diseases. I also completed
a two year Masters in Public Health (MPH) program at Walden University, USA in November 2018.

I am currently the Chief Medical Officer of the Infection Specialists of Middle Georgia, LLC, (ISMG, LLC) in Warner Robins, Georgia. I am currently affiliated with the Atrium Health Navicent Hospital and the Regency Hospital Center, both in Macon, Georgia

Global Infectious Disease Initiative 2024

Resistant Gram Negative Bacteria as Agents of Bioterrorism.

Mobolaji Ogunsakin MBChB MPH MBA FACP
Infectious Disease Physician

Evolving Resistance Patterns in Gram Negative Bacteria – A Global Problem.

- Medical Professionals worldwide are currently dealing with multi-drug resistant Gram Negative Bacteria causing difficult to treat infections.
- These bacteria utilize multiple mechanisms to evade killing by the antimicrobials that clinicians use in treating infections.
- A major cause of this evolving resistance is antibiotic pressure from clinician prescribed antibiotics.
- Recently there is growing concern that resistant gram negative bacteria could be modified and utilized as agents of bioterrorism.

The Need for a National Security Policy Against Man-made External Attack.

- The Covid-19 Pandemic taught us to prepare against pandemics arising from emerging novel viral pathogens.
- Most nations now have in place a plan to respond quickly to emerging viral outbreaks.
- Most nations also have in place a national security policy for protection in case of a man-made external attack like war.
- However, most nations don't have a national health security policy in case of a natural pathogen or a weaponized man-made bioterrorist attack.

Future Pandemics – Possible Gram negative bacteria etiology

- The world has experienced viral pandemics in the past such as the 1918 Spanish flu pandemic and the ongoing Covid-19 pandemic.
- The world has also experienced bacterial pandemics such as the "Black Death".
- "The Black Death" was a pneumonic plague pandemic that occurred in Europe from 1346 to 1353.
- It killed as many as 50 million people, 50% of Europe's population at the time.
- It was caused by Yersinia pestis, a gram negative coccobacillus bacterium.
- A weaponized strain of Yersinia pestis is a prime candidate for a present day man-made bioweapon causing a pandemic (1).

Pandemic Preparedness – The Covid-19 blueprint.

- Institutional/National/International Pandemic preparedness plans have been developed for the Covid-19 pandemic.
- National Healthcare Pandemic preparedness plans developed for the Covid-19 pandemic can be adapted for use against Gram Negative bacteria outbreaks.
- Future pandemics will hopefully result in a rapid deployment of testing and treatment resources.
- We need to consider the possibility that future pandemics may be caused by gram negative bacteria, a natural pathogen or a weaponized man-modified micro-organism.
- The WHO is playing a major role in strengthening the global health-security interface.

Concern about resistant GNR bacteria as bioterrorism agents.

- Since the September 2001 Anthrax attacks in New York city, Washington D.C. and other cities in America, concern has grown about the use of "weaponized" bacteria to attack institutions and/or countries.
- To become effective agents of bioterrorism, bacteria have to be highly infectious and be capable of causing difficult to treat infections.
- Potential candidates in this regard include the following agents:
- Francisella tularensis the causative agent of Tularemia.
- Yersinia pestis the causative agent of Pneumonic plague.

Tularemia as a bioweapon.

- Francisella tularensis, the causative agent of Tularemia, has a high infectivity rate and has been studied and prepared as a bioweapon by the USA, Russia, Japan, Britain and other countries.
- In the 1970s - 1980s, the Soviet Union conducted a focused research program with the sole purpose of creating multi-drug resistant strains of Francisella tularensis (3).
- Francisella tularensis is easily stored in dried form, can cause life-threatening infection by inhalation , and has been engineered as an antibiotic resistant organism(4).
- Although the use of biological weapons was officially prohibited by an international treaty signed in 1972, the threat of bioterrorism persists today (5).

Virulence Factors of Gram Negative bacteria.

- Many gram negative bacteria have virulence factors that enable them to evade the body's immune system and cause severe infections in affected patients.
- Endotoxins (lipopolysaccharides) in the bacterial outer membranes can trigger a cascade process in patients leading to severe sepsis and death.
- This process can cause damage to multiple body organs resulting in multiorgan failure with an associated high mortality.
- In this scenario aggressive treatment with IV antibiotics, IV fluids, pressor agents and Life support machines are needed to save the patient's life.

Antibiotic Resistance

- Many gram negative bacteria have multiple defense mechanisms that facilitate their resistance to commonly used antibiotics.
- This makes infections caused by these bacteria very difficult to treat.
- Newer expensive broad spectrum antibiotics are the only effective treatment options in this scenario such as new beta lactam/beta lactamase combinations and carbapenems.
- Low and middle income countries may not have easy access to these medications thus allowing the rapid spread of these infections without effective treatment options.

Ease of Dissemination

- Manipulation of bacterial pathogens by humans to increase their resistance to antibiotics and facilitate their ease of dissemination i.e. “weaponization”, as occurred with the anthrax attacks in Washington D.C. in 2001,
- Dissemination via water, food or aerosolized forms can make gram negative bacteria a versatile choice for nefarious purposes.
- If a small dose of the bacterium (inoculum) is required to cause an infection this means that a small quantity of bacteria can infect a large number of people. Aerosolized Yersinia pestis has this ability when it causes pneumonic plague and it can be transmitted from person to person.

High Infectivity and Mortality rate.

- Highly infectious gram negative bacteria such as Yersinia pestis, the causative agent of plague, can cause widespread morbidity and mortality especially via airborne spread in pneumonic plague which has a 100% mortality rate within 24 hours if untreated.
- Pneumonic plague can be cured by early treatment with one of these antibiotics: streptomycin, gentamicin, tetracyclines, chloramphenicol or fluoroquinolones. Resistance to these commonly used antibiotics can be induced in the laboratory in a process of weaponization.
- It is very important to determine early in the course of an outbreak if the infection is capable of airborne spread. In this scenario, the deployment of mask wearing countermeasures may significantly limit the spread of the infection as was done in the Covid -19 pandemic.

National Public Health Systems – Pandemic Preparedness – Details.

- Preparation for and mitigation of risks associated with infections caused by resistant gram negative bacteria.
- Vigilance, Awareness and strong National political will are needed to develop adequate National Public Health Systems.
- Maintenance of Robust surveillance systems is key to early detection of outbreaks.
- Development and deployment of rapid detection methods nationwide is key.
- Ensuring availability of effective countermeasures requires the deployment of significant national resources.

Countermeasures

- Development of strategies to combat antibiotic resistance.
- Development of new antibiotics to target resistant gram negative bacteria.
- Rapid development and deployment of novel global vaccines.
- International healthcare collaboration programs between nations.

An Urgent Public Health problem.

- Continuous spread of antimicrobial resistance, especially antibiotic resistance and the lack of newly developed antibiotics.
- Antibiotic use and misuse drive the development of antibiotic resistance.
- The situation is compounded in developing countries by the presence of unregulated supply chains and the absence of a systematic drug prescription program.
- The use of antibiotics as growth promoters in the food animal production industry has further compounded the problem of emerging antibiotic resistance in bacterial pathogens.

References

- 1.Int J Health Sci (Qassim). 2022 May-Jun; 16(3): 1-3: Future pandemics might be caused by bacteria and not viruses: Recent advances in medical preventive practice.
- 2. Green MS, LeDuc J, Cohen D, Franz DR. Confronting the threat of bioterrorism: realities, challenges, and defensive strategies. *Lancet infect Dis* 2019; 19:e2-e13.
- 3. Hoffman D. *The dead hand: the untold story of the cold war arms race and its dangerous legacy.* New York, NY: Doubleday, 2009.
- 4. World Health Organization. *WHO Guidelines on tularemia*. World Health Organization. https://iris.who.int/handle/10665/43793. 2007.
- 5. "Status of the Biological Weapons Convention" United Nations Office for Disarmament Affairs. Retrieved 3 July 2024.

THANK YOU

SPEAKER'S PROFILE

DR. IORHEN E. AKASE

Head, Infectious Diseases College of Medicine
UNILAG

Dr IE Akase has expertise managing patients with infectious diseases, including infectious diseases with epidemic potential such as Lassa fever, MPOX, and COVID-19, as well as patients with HIV, tuberculosis (TB), and sepsis. Dr Akase has sub-specialty training in infectious diseases and immunology, having earned a Master's degree in immunology and a post-graduate fellowship in infectious diseases (ID). His work during his MSc and fellowship programs prepared him for some of the current clinical and research initiatives.

For the past six years, Dr Akase has been a member of various technical working groups, including the Public Health Emergency Operations Center in Lagos State, where the majority of the outbreaks have occurred. In addition, he currently chairs the Nigerian Infectious Diseases Society's (NIDS) Epidemic Response Committee, and is a member of the committee for the development of the National guideline for the clinical management of COVID-19, as well as the committee for the development of COVID-19 training modules. He also chaired the Oyo State committee for isolation facility accreditation and currently serves on the board of the Pan-African Mycology Working Group (PAMG) of the International Society for Human and Animal Mycology (ISHAM). Dr. Akase has had ample opportunities to collaborate closely with government and other implementing partners, gaining significant expertise and forging enduring networks in the process. He has worked with many other researchers and clinicians to publish over 40 manuscripts in respected international and national journals, and looks forward to leveraging his experience and extensive networks among colleagues to help the country and global partners achieve their collective goals.

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APPRECIATION

The entire TEAM of Global Infectious Diseases Initiative Inc., wishes to express our profound gratitude to all who attended our 4th GIDI Lectures.

We extend our sincere appreciation to all our supporters, friends, well-wishers, organizations and individuals who have assisted us in making this event a great success.

Thank you and God bless.

Signed:
Dr. Folarin Adegboyega Olubowale
MD/CEO, Global Infectious Diseases Initiative