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ASLM CPD SERIES · DIAGNOSTIC TECHNOLOGIES & EPIDEMIOLOGICAL TOOLS

Bacterial Genetics and the Emergence and Spread of AMR

From the gene, to the plasmid, to the patient — and what it means for Africa

Edwin Kamau, PhD, ABMM, ASCP
Senior Director, Medical Scientific Affairs
July 31, 2026

LEARNING OBJECTIVES

By the End of This Session, You Will Be Able To

- Describe how mutation and horizontal gene transfer generate antimicrobial resistance
- Explain plasmid structure and biology, and why plasmids — not the chromosome — drive the global AMR pandemic
- Summarize the global and African AMR burden, and the WHO priority pathogens most relevant to your bench
- Articulate why AMR is treated as a global health-security issue, and what policy frameworks exist
- Describe the clinical microbiologist's role in diagnosis, diagnostic stewardship, and clinician partnership in low-resource settings

Roadmap for Today

Genetics Foundations - Chromosome, mutation vs. horizontal gene transfer, mechanisms of resistance

Plasmids & Mobile Genetic Elements - Structure, conjugation, Inc groups, virulence–resistance convergence

Global & African AMR Burden - GBD estimates, WHO priority pathogens, MAAP diagnostic gap data

AMR as Global Health Security - Why it meets the security threshold, policy architecture, NAPs

Guidelines in Practice - AWaRe, GLASS/GLASS-EAR, CLSI/EUCAST, One Health governance

The Clinical Microbiologist's Role - Diagnostics, diagnostic stewardship, clinician partnership in LRS

Every antibiotic failure at the bedside began as a single base change — or a single plasmid — years earlier, somewhere else.

AMR has been called a “silent pandemic.” Today we make it visible — from the gene to the patient.

The “silent pandemic” framing follows the Interagency Coordination Group on Antimicrobial Resistance report to the UN Secretary-General, 2019, and the O'Neill Review on Antimicrobial Resistance, UK Government, 2016.

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SECTION 1

Genetics Foundations: From Basic Genetics to Bacterial Genetics

How a genome built for speed becomes a genome built for resistance

The Bacterial Genome, Briefly

- A single circular (usually), haploid chromosome — typically 1–6 megabases, no nuclear envelope
- No sexual reproduction: each division simply copies the genome — but generation time can be as short as 20–30 minutes
- Huge population sizes + rapid turnover mean that even rare mutational events are tested by selection constantly
- Contrast with human genetics: haploid, asexual, populations in the billions per infection — this is why resistance evolves on a clinical, not evolutionary, timescale

General bacterial genetics; see Blair JM, Webber MA, Baylay AJ, Ogbolu DO, Piddock LJV. Molecular mechanisms of antibiotic resistance. Nat Rev Microbiol. 2015;13(1):42–51.

Two Roads to Resistance

Vertical Evolution

- Spontaneous chromosomal mutation, then selection
- e.g. rpoB mutations → rifampicin resistance
- e.g. gyrA/parC mutations → fluoroquinolone resistance
- e.g. porin loss → reduced carbapenem entry in Klebsiella
- Slow, stepwise, confined to one lineage

Horizontal Gene Transfer (HGT)

- Acquisition of pre-formed resistance genes from other bacteria
- Dominant route for clinically important multidrug resistance
- Can move complete, functional resistance across species — and even genera
- Converts a resistance event from decades to days
- The reason a gene can appear in an unrelated pathogen almost overnight

Munita JM, Arias CA. Mechanisms of Antibiotic Resistance. Microbiol Spectr. 2016;4(2); von Wintersdorff CJH, et al. Dissemination of Antimicrobial Resistance through Horizontal Gene Transfer. Front Microbiol. 2016;7:173.

Mechanisms of Horizontal Gene Transfer

- Transformation — uptake of naked, free DNA from the environment
- Transduction — phage (bacteriophage)-mediated transfer of DNA between bacteria
- **Conjugation — direct cell-to-cell transfer via a pilus, almost always plasmid-borne**
  - ❑ Conjugation is the clinically dominant mechanism for AMR spread
  - ❑ It can move large, multi-gene cassettes across species and genera in a single mating event — which is exactly why plasmids are the focus of Section 2

Von Wintersdorff CJH, et al. Front Microbiol. 2016;7:173; Virolle C, et al. Plasmid Transfer by Conjugation in Gram-Negative Bacteria. Genes. 2020;11(11):1239.

Four Biochemical Mechanisms of Resistance

- Enzymatic inactivation — e.g. β-lactamases (ESBLs, NDM, OXA-48), aminoglycoside-modifying enzymes
- Target modification — mecA → altered penicillin-binding proteins, ribosomal protection, DNA gyrase mutation
- Reduced permeability — porin loss limiting drug entry (classic in carbapenem resistance)
- Efflux pumps — active expulsion of the drug before it can act
    - ❑ Mobile genetic elements are especially efficient at carrying mechanisms 1 and 4 between unrelated species

Munita JM, Arias CA. Mechanisms of Antibiotic Resistance. Microbiol Spectr. 2016;4(2); Reygaert WC. An overview of the antimicrobial resistance mechanisms of bacteria. AIMS Microbiol. 2018;4(3):482–501.

Mobile Genetic Elements: The Vehicles of HGT

- Plasmids — self-replicating extrachromosomal DNA; the dominant vehicle for clinical AMR
- Transposons ("jumping genes") — mobile segments that relocate within or between DNA molecules
- Integrons — gene-capture platforms that assemble cassettes of resistance genes
- Insertion sequences — the simplest mobile elements, often flanking resistance genes
  - ❑ If resistance genes are cargo, mobile genetic elements are the trucks, ships, and containers — and plasmids are the ships that carry many containers at once and dock in many ports (species).

Partridge SR, Kwong SM, Firth N, Jensen SO. Mobile Genetic Elements Associated with Antimicrobial Resistance. Clin Microbiol Rev. 2018;31(4):e00088-17.

Why This Matters Clinically: Co-Selection

- A single plasmid can carry resistance genes to several unrelated drug classes — plus heavy-metal or disinfectant resistance — on the same cassette
- Using just one antibiotic (or even a biocide/disinfectant) can therefore co-select for resistance to several others simultaneously
  - ❑ This is a key reason narrow, single-drug stewardship interventions sometimes underperform expectations — the resistance genes are traveling together

Baker-Austin C, Wright MS, Stepanauskas R, McArthur JV. Co-selection of antibiotic and metal resistance. Trends Microbiol. 2006;14(4):176–182.

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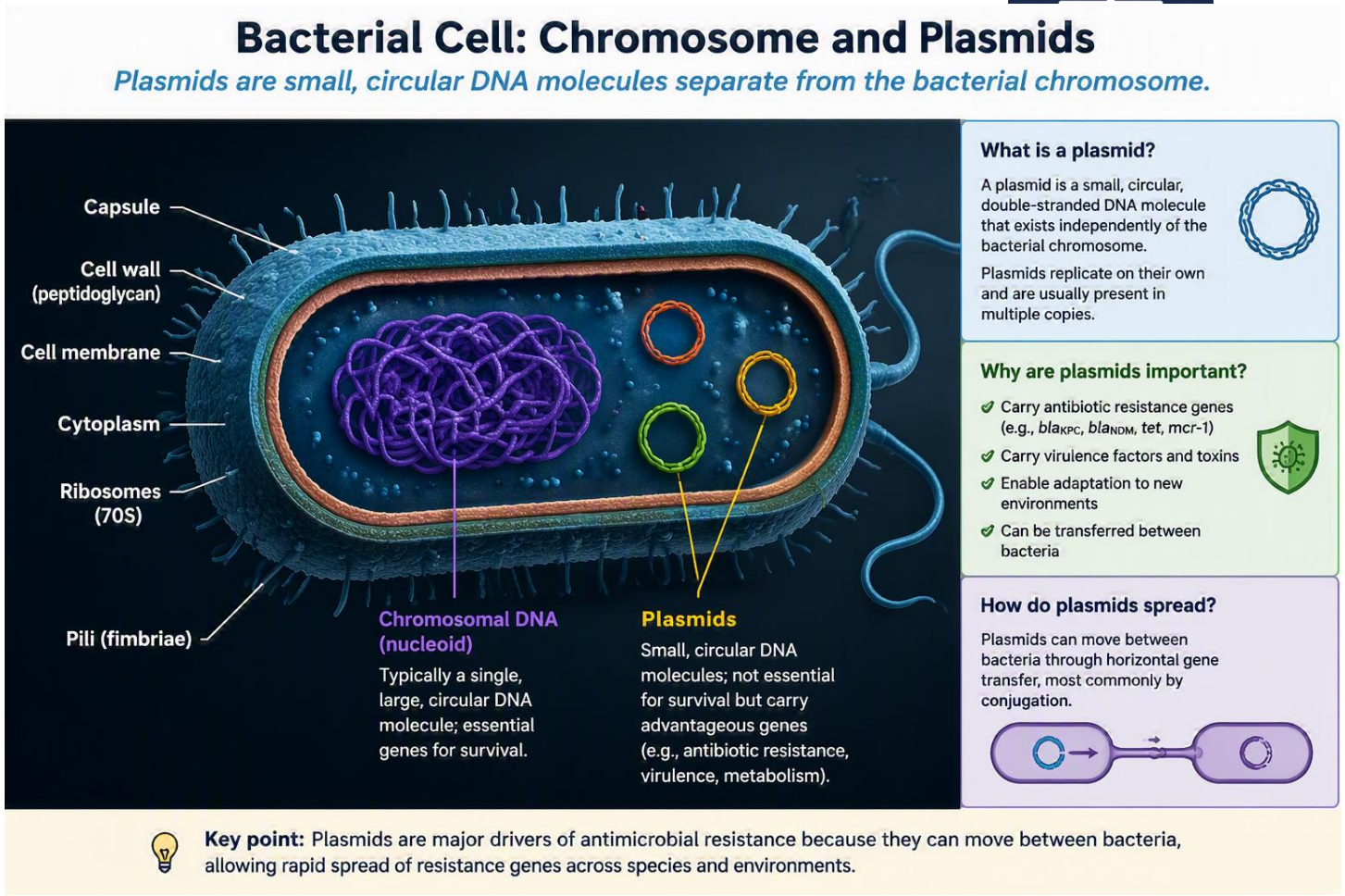
SECTION 2

Plasmids: Structure, Biology, and Role in AMR

The single most important vehicle for the global spread of antimicrobial resistance

What Is a Plasmid?

- Extrachromosomal, self-replicating, typically circular double-stranded DNA
- Ranges from a few kb to over 500 kb (“megaplasmids”)
- Not essential for bacterial survival — but confers major selective advantage under antibiotic pressure
- Enormous diversity: the PLSDB reference database recorded over 72,000 non-redundant plasmid sequences by mid-2024



Schmartz GP, et al. Challenges and considerations for whole-genome-based antimicrobial resistance plasmid investigations. 2024 (PLSDB plasmid database); Carattoli A. Plasmids and the spread of resistance. Int J Med Microbiol. 2013;303(6–7):298–304.

Anatomy of an AMR Plasmid

Mobile genetic elements that drive the spread of antimicrobial resistance

1 BACKBONE

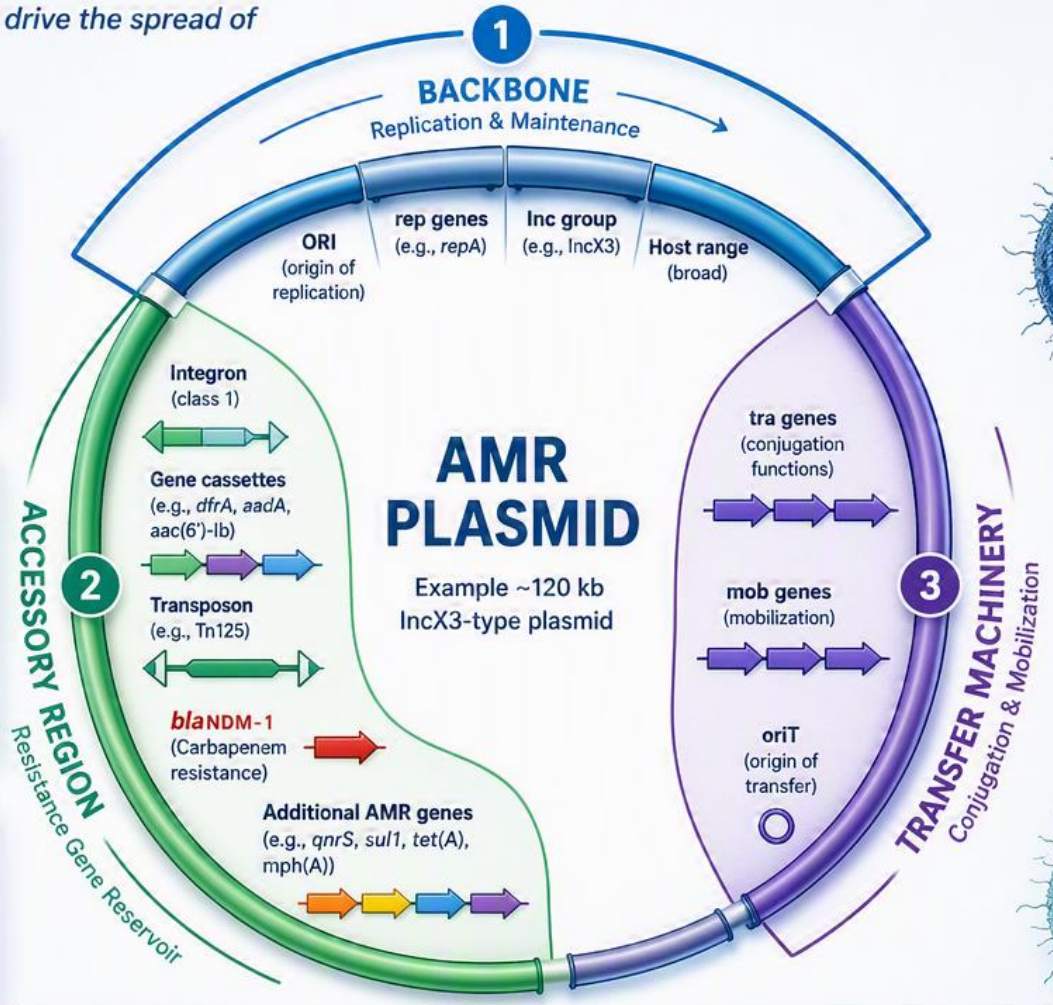
origin of replication + *rep* genes define the plasmid's Inc group and host range.

2 ACCESSORY REGION

resistance genes are frequently clustered inside integrons or transposons for efficient capture and shuffling.

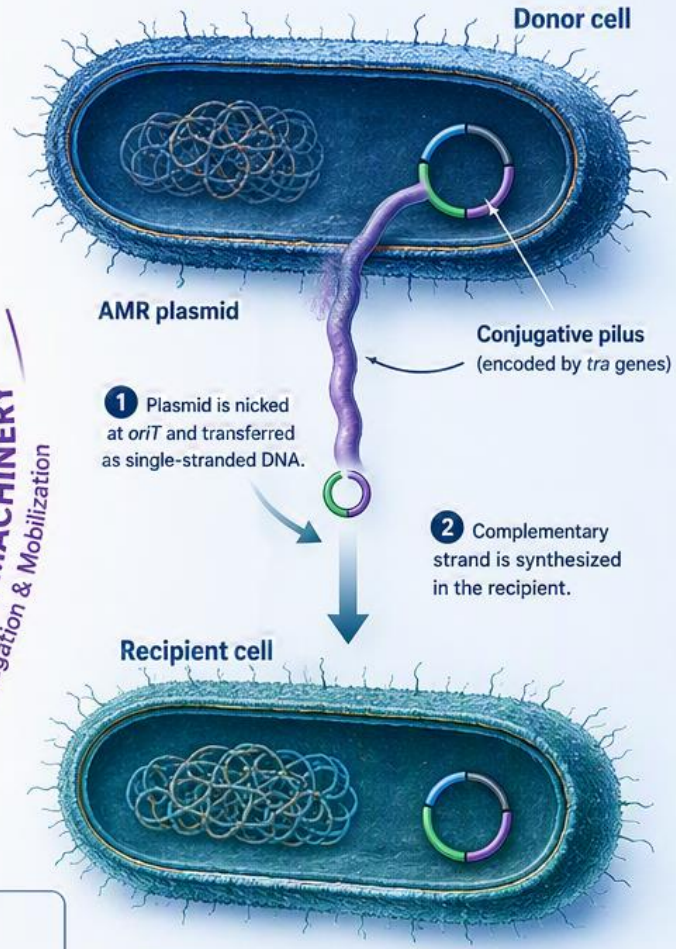
3 TRANSFER MACHINERY

tra/mob genes and a conjugative pilus allow self-mobile plasmids to move between cells — and even between species and genera.



HORIZONTAL GENE TRANSFER via CONJUGATION

Self-mobile plasmids can move between bacteria through a conjugative pilus.



REPLICATION

ORI and *rep* genes ensure faithful replication and stable inheritance.

CONJUGATION

Transfer machinery mediates transfer via a pilus.

HORIZONTAL GENE TRANSFER

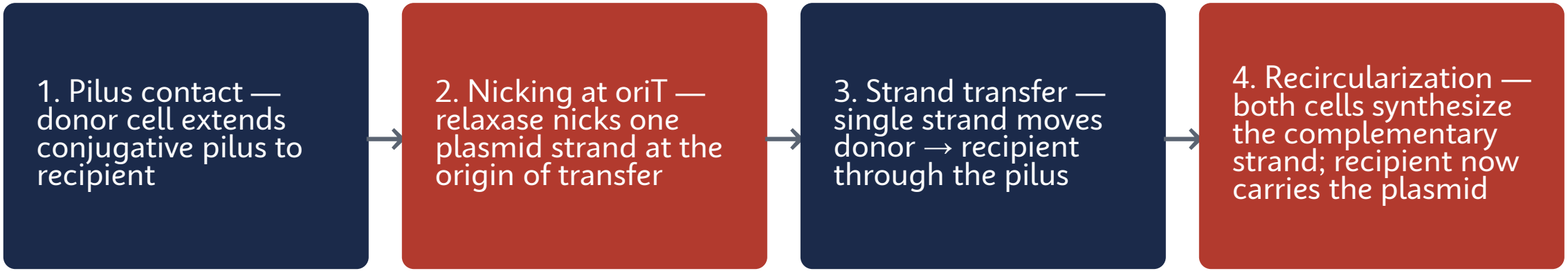
Enables spread of AMR genes across species and genera.

LEGEND

- Backbone (Replication & Maintenance)
- Accessory Region (Resistance Gene Reservoir)
- Transfer Machinery (Conjugation & Mobilization)
- Key AMR Gene (e.g., *bla*NDM-1)
- Gene or functional element
- *oriT* (origin of transfer)

Key driver of the dissemination of antimicrobial resistance in clinical and environmental settings.

Conjugation in Action



Clinically dominant HGT mechanism for AMR: conjugative plasmids move large resistance-gene cassettes across species and even genera in a single mating event — explaining how a gene first seen in one organism can appear in an unrelated pathogen within one hospital ward.

Virolle C, Goldlust K, Djermoun S, Bigot S, Lesterlin C. Plasmid Transfer by Conjugation in Gram-Negative Bacteria. Genes (Basel). 2020;11(11):1239.

Incompatibility (Inc) Groups: Epidemic Plasmid “Chassis”

- IncF, IncN, IncA/C, IncX, IncH — different replicon “chassis” favor different gene cargo and host ranges
- Certain Inc-group plasmids have become globally epidemic vehicles for specific resistance genes
  - ❑ Think of it as “successful clones” — but at the plasmid level, not the bacterial level: the same plasmid backbone can turn up in unrelated species on different continents

Carattoli A. Plasmids and the spread of resistance. Int J Med Microbiol. 2013;303(6–7):298–304.

The Clinical Greatest Hits — What Plasmids Actually Carry

- ESBLs — blaCTX-M, blaTEM, blaSHV (third-generation cephalosporin resistance)
- Carbapenemases — blaNDM, blaKPC, blaOXA-48
- Colistin resistance — mcr-1 through mcr-10
- Fluoroquinolone/aminoglycoside resistance — qnr genes, aac(6')-Ib-cr
  - ❑ These are overwhelmingly plasmid- or MGE-borne — precisely why they achieved global, multi-species distribution instead of staying confined to one clone or one country

Bush K, Bradford PA. Epidemiology of β-Lactamase-Producing Pathogens. Clin Microbiol Rev. 2020;33(2):e00047-19; Liu YY, et al. Emergence of plasmid-mediated colistin resistance mechanism mcr-1. Lancet Infect Dis. 2016;16(2):161–168.

Fitness Cost and Compensatory Evolution

- Carrying a plasmid is metabolically costly; bacteria without benefit are often outcompeted absent antibiotic pressure
- But compensatory mutations — and co-selection (Section 1) — frequently erase this cost
  - ❑ This is why resistance often persists even after the selecting antibiotic is withdrawn — a sobering point for anyone hoping stewardship alone reverses resistance quickly

Vogwill T, MacLean RC. The genetic basis of the fitness costs of antimicrobial resistance: a meta-analysis approach. Evol Appl. 2015;8(3):284–295.

When Virulence and Resistance Converge on the Same Plasmid

- The newest and most alarming development in Gram-negative genetics: hybrid plasmids carrying both virulence and resistance genes
- Virulence cargo: siderophore systems (aerobactin, iucABCD), capsule regulators (rmpA/rmpA2), metabolic transporter peg-344
- Resistance cargo on the same element: blaKPC, blaNDM, blaOXA-48 carbapenemases
  - ❑ This converts organisms that were previously either “highly virulent but treatable” or “resistant but not very invasive” into strains that are both — the convergent, carbapenem-resistant hypervirulent Klebsiella pneumoniae (CR-hvKp) phenomenon

Russo TA, Marr CM. Hypervirulent Klebsiella pneumoniae. Clin Microbiol Rev. 2019;32(3):e00001-19; Tian T, et al. A systematic review of hypervirulent Klebsiella pneumoniae research. Front Med (Lausanne). 2025;12:1545678.

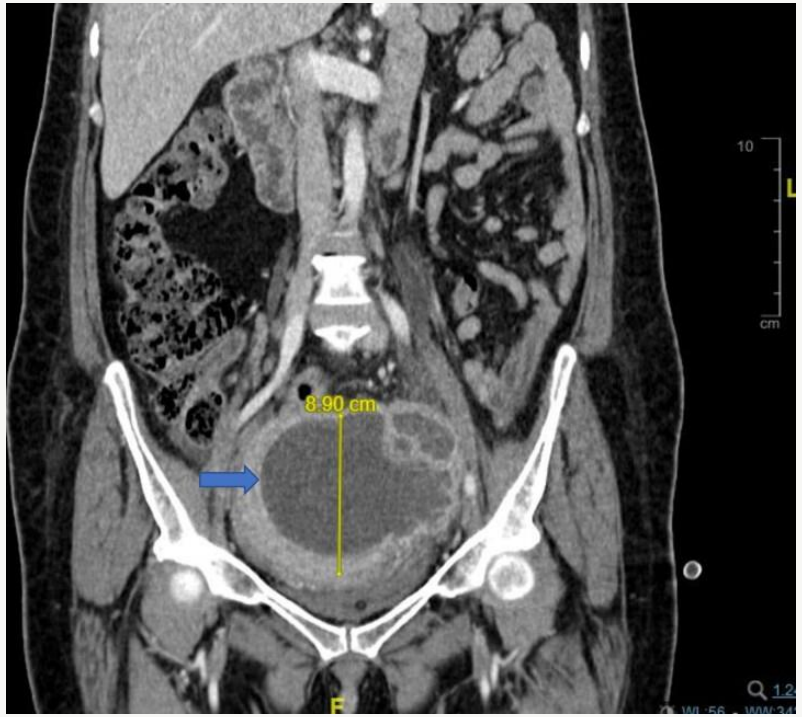
CASE STUDY

1

52-year-old woman, poorly controlled type 2 diabetes (HbA1c 12.3%) and hypertension. Four months of recurrent pelvic pain and vaginal discharge, repeatedly treated as recurrent UTI before presenting with urinary retention and a 12.2 cm pelvic mass suspicious for malignancy.

Genetics Made Visible at the Bedside

- Recurrent *E. coli* / *Klebsiella pneumoniae* UTIs over months, each treated empirically — no isolate characterized beyond routine AST
- Blood cultures ultimately grew hypervirulent *K. pneumoniae* (hvKp); exploratory laparotomy found a myometrial abscess, not malignancy
- The organism's hypermucoviscosity and metastatic-spread behavior trace directly to plasmid-borne iucA / iroB / peg-344 / rmpA / rmpA2 — the exact genes just discussed



This is the genetics from the last five slides, walking into your clinic. A plasmid map became a patient's four-month diagnostic odyssey.

Presenter's own case (UCLA, 2021) — replace with your own citation/case number if presenting the published report.

CASE STUDY

2

Clinical Case Overview

A 30-year-old diabetic patient developed severe eye infection with multiple invasive symptoms and complex diagnosis.

Endogenous Endophthalmitis Caused by ST66-K2 Hypervirulent *Klebsiella pneumoniae*

- Microbiological Findings

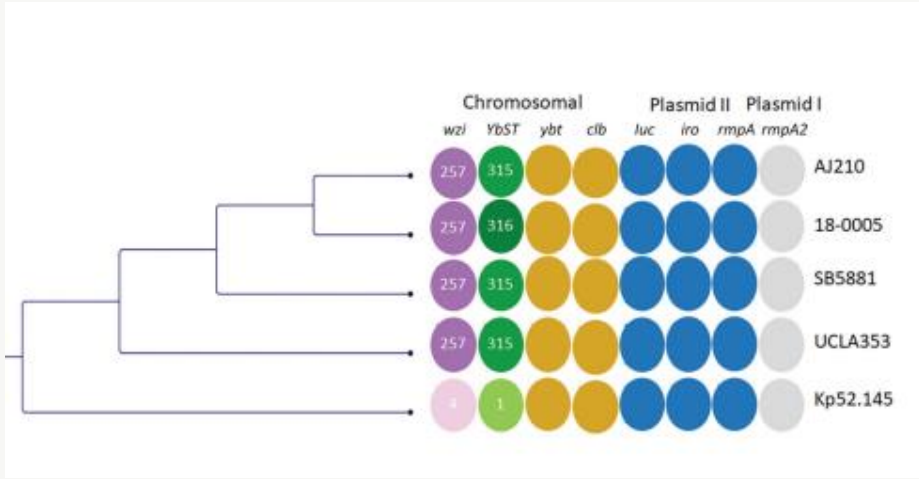
The *Klebsiella pneumoniae* isolate was hypervirulent, susceptible to antibiotics, and lacked resistance genes on genome sequencing.

- Genomic Virulence Features

Genome analysis revealed conserved virulence genes explaining hypermucoviscous phenotype and immune system evasion.

- Clinical Outcome and Implications

Despite aggressive treatment, the patient suffered severe vision loss, underscoring hypervirulence risks beyond antimicrobial resistance.



This is what happens when virulence genes leave the genome and enter the patient's story. A bacterial lineage preserved for nearly a century changed the course of a young man's life.

Presenter's own case (UCLA, 2020) — published as Kamau et al., Endogenous Endophthalmitis Caused by ST66-K2 Hypervirulent Klebsiella pneumoniae, United States. Emerg Infect Dis. 2021;27(8):2215–2218*

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SECTION 3

The Global and African AMR Crisis

Sizing the problem — and the diagnostic gap that hides its true scale

SECTION 3 · BURDEN

Sizing the Global Problem

4.95M

Deaths associated with bacterial AMR globally in 2019

1.27M

Deaths directly attributable to resistance — more than malaria or HIV in the same analysis

2050

Forecast horizon for continued mortality growth without intervention

AMR is not a future threat — by these estimates, it is already among the leading causes of death worldwide.

Murray CJL, et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet. 2022;399(10325):629–655; Naghavi M, et al. Global burden of bacterial antimicrobial resistance 1990–2021, forecasts to 2050. Lancet. 2024;404(10459):1199–1226.

SECTION 3 · BURDEN

Africa Carries a Disproportionate Share

19.6%

Median resistance across infections in the African Region (GLASS 2025)

17.2%

Global median resistance for comparison

↑

Likely an underestimate — so little of Africa's clinical bacteriology is captured in surveillance at all

The WHO African Region cross-country analysis found the region's AMR mortality burden among the highest of any WHO region.

Sartorius B, et al. The burden of bacterial antimicrobial resistance in the WHO African region in 2019: a cross-country systematic analysis. Lancet Glob Health. 2024;12(2):e201–e216; Antimicrobial resistance landscape in Africa: Perspectives from the WHO GLASS report 2025.

The Diagnostic Gap Behind the Numbers

- **MAAP (Mapping AMR and Antimicrobial Use Partnership, Fleming Fund/ASLM): >50,000 labs reviewed across 14 sub-Saharan African countries**
- Only ~1.3% of laboratories could perform basic bacteriology testing
- Under 30% had any access to antimicrobial susceptibility testing (AST)
- Lancet Microbe/LSHTM spotlight: only 23% of surveyed labs ISO 15189-accredited; only 15% used any electronic laboratory information system
  - ❑ This is the diagnostic infrastructure the rest of this talk's final section will address

Ondoa P et al., (2025). Bacteriology testing and antimicrobial resistance detection capacity of national tiered laboratory networks in sub-Saharan Africa: an analysis from 14 countries. The Lancet Microbe, 6(1), 100976.

WHO Bacterial Priority Pathogens List (BPPL) 2024

Critical Tier

- Carbapenem-resistant *Klebsiella pneumoniae* — ranked #1 of 24 pathogens (84% score)
- Carbapenem-resistant Acinetobacter baumannii
- 3rd-generation cephalosporin-resistant Enterobacterales (3GCRE) — new standalone category in 2024
- 3GCRE addition reflects its outsized burden in neonatal sepsis in LMICs

High Tier — Community-Acquired

- Fluoroquinolone-resistant *Salmonella* Typhi
- Shigella spp.
- *Neisseria gonorrhoeae*
- Elevation reflects community-acquired resistance tied to water/sanitation gaps — directly relevant to African epidemiology

WHO Bacterial Priority Pathogens List, 2024 (WHO/IRIS, publication 9789240093461); The WHO Bacterial Priority Pathogens List 2024: a prioritisation study to guide research, development, and public health strategies. 2025.

Regional Data Snapshots: Enterobacterales in Africa

- **Central Africa systematic review/meta-analysis (2008–2024, 9 countries):**
  - ❑ Pooled ESBL-producing Enterobacterales prevalence of 22% (41% in carriage, 10% in clinical isolates)
- **Sub-Saharan African pediatric meta-analysis:**
  - ❑ Substantial burden of 3rd-gen cephalosporin- and carbapenem-resistant Enterobacterales among children — a population with the least room for empiric-therapy error

Antimicrobial resistance of Enterobacterales in Central Africa: a systematic review and meta-analysis. Commun Med. 2025; Antimicrobial resistance in Enterobacterales infections among children in sub-Saharan Africa: a systematic review and meta-analysis. eClinicalMedicine. 2024.

Why Africa Is Vulnerable — Drivers, Not Just Numbers

- Unregulated antibiotic access and widespread self-medication
- Weak stewardship infrastructure and limited laboratory workforce
- National AMR Action Plans that, on average, allocate only ~12% of interventions to laboratory/bacteriology capacity
    - ❑ This is a systems failure, not an individual-behavior failure

MAAP report, Fleming Fund/ASLM, 2024; Godman B, et al. Tackling antimicrobial resistance across sub-Saharan Africa: current challenges and implications for the future. Expert Opin Drug Saf. 2022;21(8):1089–1111.

CASE STUDY

3

Retrospective whole-genome sequencing analysis of carbapenem-resistant *Klebsiella pneumoniae* isolates collected from Djibouti city, Djibouti, East Africa.

Africa-Specific Genomics: The Convergence Phenomenon Is Already Here

- Of 32 carbapenem-resistant *K. pneumoniae* isolates sequenced, 12.5% (4/32) were carbapenem-resistant hypervirulent *K. pneumoniae* (CR-hvKp)
- This is the same hybrid virulence-resistance plasmid phenomenon described in Section 2 — detected only because a whole-genome-sequencing partnership existed
  - ❑ The open question this case forces: how many similar strains are circulating undetected where no such sequencing partnership exists?

The convergence of hypervirulence and carbapenem resistance is not a Northern-hemisphere hypothetical — it is already circulating in African hospitals.

Galal L et al., Circulation of hypervirulent carbapenem-resistant Klebsiella pneumoniae in humans and fish in Djibouti. J Antimicrob Chemother. 2024 Aug 1;79(8):2068-2071.

029

SECTION 4

AMR as a Global Health Security and Policy Issue

A problem killing more people than malaria and HIV combined in some analyses, crossing borders through travel, trade, food, and the environment is no longer only a clinical problem — it is a matter of national and global security.

Why AMR Meets the Definition of a Security Threat

- Cross-border spread via travel, trade, and food supply chains
- Capacity to undermine the foundations of modern medicine — surgery, chemotherapy, transplantation, and neonatal care all depend on effective antibiotics
- Documented potential for rapid international dissemination of resistant clones and plasmids — the 2024–2025 WHO hvKp Disease Outbreak News and Rapid Risk Assessment are a direct, recent example
  - ❑ This is the same logic that placed pandemic preparedness on G7/G20 and UN Security Council agendas

WHO Disease Outbreak News: Hypervirulent Klebsiella pneumoniae, Dec 2024; WHO Rapid Risk Assessment — Hypervirulent Klebsiella pneumoniae, Global, 2025.

The Global Policy Architecture

- WHO Global Action Plan on AMR (2015) — the framework nearly all National Action Plans derive from
- The Quadripartite (WHO–FAO–WOAH–UNEP) One Health collaboration
- 2016 and 2024 UN General Assembly High-Level Meetings on AMR — member states committed to reducing global AMR-associated human deaths by a stated target by 2030
  - ❑ An honest, evidence-based caveat: political commitments have consistently outpaced funded implementation

WHO Global Action Plan on Antimicrobial Resistance, 2015; UN General Assembly Political Declaration of the High-Level Meeting on AMR, 2016 and 2024.

National Action Plans: Aspiration vs. Implementation

- Near-universal formal adoption of National AMR Action Plans — but highly uneven implementation
- East African Community progress against WHO's own checklist ranged from 44% (South Sudan) to 94% (Kenya)
- **Across Africa broadly, only ~12% of NAP interventions target laboratory/bacteriology capacity**
- Plans that look complete on paper often under-resource the exact diagnostic function this talk is about

Molina A, et al. Strategies and challenges in containing antimicrobial resistance in East Africa: a focus on laboratory-based surveillance. Antimicrob Resist Infect Control. 2025;14:134; MAAP report, Fleming Fund/ASLM, 2024.

Regional and Continental Mechanisms (Africa-Specific)

- Africa CDC AMR Surveillance Network (AMRSNET) — standardizing surveillance across Africa CDC, WHO GLASS, ECOWAS, ECSA-HC
- The Fleming Fund — supporting AMR surveillance capacity across East and Southern Africa
- Global Fund's 2025 investment: ~US$294M in diagnostics and ~US$200M in laboratory system strengthening in Africa
- ASLM's continental laboratory-strengthening mandate — the very organization convening this CPD series

Africa CDC AMRSNET first-edition guidance, Sep 2024; Global Fund resilient and sustainable systems for health strategy, 2025; ASLM programmatic reporting.

One Health Governance

- AMR does not respect the human–animal–environment boundary
- Agricultural/veterinary antibiotic use, environmental antibiotic residues, and human clinical use all feed the same resistance gene pool
  - ❑ The same conjugative plasmids from Section 2 move between human, animal, and environmental bacteria — which is exactly why a purely clinical response cannot solve this

James R, Hardefeldt LY, Ierano C, et al. Antimicrobial stewardship from a One Health perspective. Nat Rev Microbiol. 2025; OECD. Embracing a One Health Framework to Fight Antimicrobial Resistance. OECD Health Policy Studies, 2023.

Guidelines That Operationalize Policy at the Bedside

- WHO AWaRe classification (Access / Watch / Reserve) — for rational prescribing
- WHO Global AMR Surveillance System (GLASS) and its GLASS-EAR (Emerging AMR) reporting stream — how signals like the hvKp convergence actually reach global attention
- CLSI / EUCAST breakpoints — the technical backbone that makes AST results comparable across labs and countries

❑ All of this is only actionable if a clinical microbiologist can detect it and communicate it — which is where we go next

WHO AWaRe classification framework; WHO Global Antimicrobial Resistance and Use Surveillance System (GLASS) methodology, 2024; CLSI M100 Performance Standards for Antimicrobial Susceptibility Testing.

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SECTION 5

The Clinical Microbiologist's Role

Diagnostics, diagnostic stewardship, and clinician partnership — especially in low-resource settings

From Gene to Guideline to Bedside: Closing the Loop

- Mutation/HGT (Section 1) → plasmid-mediated spread (Section 2) → measurable regional/global burden (Section 3) → policy response (Section 4)
  - ❑ … and all of it is only actionable if a clinical microbiologist can detect it and communicate it in time
- This is the thesis of this closing section

Why Routine Phenotypic Methods Are Necessary but Not Sufficient

- Standard culture and AST do not detect virulence determinants or definitively identify carbapenemase mechanism
- Genotypically similar-looking isolates can have very different clinical trajectories — hvKp and classical *K. pneumoniae* look alike on a plate
- **Practical answer for low-resource settings — a tiered, resource-matched diagnostic ladder:**
- String test and phenotypic carbapenemase screens (e.g. modified Hodge / carbapenem inactivation methods) as affordable first-line tools
- Referral pathways to PCR- or WGS-capable reference labs for confirmation of unusual or high-stakes isolates

CLSI M100 Performance Standards for Antimicrobial Susceptibility Testing; Catalán-Nájera JC, et al. Hypervirulence and hypermucoviscosity: two different but complementary Klebsiella phenotypes. Virulence. 2017;8(7):1111–1123.

Point-of-Care and Syndromic Molecular Platforms as Equalizers

- GeneXpert/BioFire-class syndromic panels can bring carbapenemase-gene detection (NDM, KPC, OXA-48) and pathogen ID within reach of district-level labs
- Opportunity: speed, minimal hands-on skill required, no need for a full genomics unit
  - ❑ Constraint, stated honestly: cost per test, cartridge supply chains, and the need to adapt panels to markers relevant to African epidemiology rather than only importing panels designed for high-income settings

In low-resource nations, lack of diagnostics hampers fight against antimicrobial resistance. CIDRAP, 2023 (bioMérieux/Fleming Fund partnership); manufacturer platform documentation, GeneXpert/BioFire.

Diagnostic Stewardship as the Precondition for Antimicrobial Stewardship

- **Antimicrobial stewardship programs cannot function without a working bacteriology service — you cannot de-escalate, target, or stop therapy you cannot characterize**
- A feasibility study at a large Ethiopian referral hospital demonstrated that a practical, CLSI-based laboratory-strengthening bundle could establish sustainable clinical bacteriology and directly support stewardship
- Proof that this is achievable in low-resource settings — not just aspirational

Diagnostic Bacteriology in District Hospitals in Sub-Saharan Africa. Front Med (Lausanne). 2019; A Feasible Laboratory-Strengthening Intervention Yielding a Sustainable Clinical Bacteriology Sector to Support Antimicrobial Stewardship in a Large Referral Hospital in Ethiopia, 2020.

Closing the Communication Gap — and Building the Workforce

- Even where bacteriology exists, laboratory staff often have limited influence on prescribing decisions, and clinicians under-utilize culture/AST results
- **Concrete, low-cost, evidence-based fixes:**
- Regular “meet-the-clinician” case rounds; cumulative antibiograms distributed to wards; lab staff embedded in ward rounds or stewardship committees; simplified — not dumbed-down — reporting formats
- **Workforce and network building:**
- Africa CDC / Africa PGI genomics and bioinformatics workshops (Ghana, 2024); WITS TB-genomics training extending to other AMR pathogens; structured CPD programs including this ASLM series itself
- **Every participant in this room is part of closing the diagnostic gap quantified in Section 3**

Diagnostic Bacteriology in District Hospitals in Sub-Saharan Africa. Front Med (Lausanne). 2019; Africa CDC Pathogen Genomics Initiative programmatic reporting, 2024.

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SECTION 6

Closing the Loop:
One More Case, and a Call to Action

CASE STUDY

4

72-year-old man after craniofacial cancer resection/reconstruction developed skull-base dehiscence, retained titanium hardware, and persistent P. aeruginosa osteomyelitis that evolved to XDR during therapy.

CLOSING CASE · DIAGNOSTICS, GENOMICS, AND CLINICIAN PARTNERSHIP

Hypermutator XDR Pseudomonas Osteomyelitis Cleared with Phage + Cefiderocol

ST782 | mutS H21P | EPa22 phage | cefiderocol

Clinical problem: Serial cultures shifted from susceptible to progressively drug-resistant P. aeruginosa despite multiple antibiotic courses, debridement, and partial hardware removal.

Genomics made failure visible: WGS showed a rare ST782 lineage, no acquired resistance genes, and a non-synonymous mutS H21P mismatch-repair mutation consistent with a hypermutator phenotype.

Actionable diagnostic bridge: Phage susceptibility testing identified EPa22, a lytic phage with activity against most patient isolates; therapy proceeded under FDA Single Patient IND / emergency use.

Outcome signal: Two weeks of twice-daily IV EPa22 plus cefiderocol was associated with normalized ESR/CRP within 1 week and microbiologic clearance of P. aeruginosa from wound culture.

This is the full AMR loop: *sequencing explained failure, susceptibility testing made rescue therapy possible, and lab–clinician coordination moved an investigational option to the bedside.*

Ngauy V, et al. Clearance of hypermutator XDR Pseudomonas osteomyelitis and hardware infection with adjunctive bacteriophage therapy. ASM Case Reports. 2026;2(2):e00108-25.

CASE STUDY

5

XDR Escherichia coli ST410 cUTI in a Returning Traveler: Genomics Changed the Risk Assessment

76-year-old returning traveler with complicated UTI after hospital care in Dubai; urine culture grew extensively drug-resistant E. coli ST410 carrying blaNDM-5 and blaCTX-M-15.

Returning traveler | cUTI | ST410 | blaNDM-5 | blaCTX-M-15 | cefiderocol R

- **Clinical trigger:** Initial empiric ceftriaxone was started before full travel/exposure history was available; admission urine culture grew extensively resistant E. coli.
- **Genomic signal:** WGS identified E. coli ST410 with blaNDM-5 and blaCTX-M-15, a high-risk clone associated with international spread and difficult-to-treat CRE.
- **Therapeutic pivot:** ID recommended ceftazidime/avibactam plus aztreonam for suspected metallo-beta-lactamase activity; fosfomycin enabled oral completion after systemic complications were excluded.
- **System response:** Microbiology, ID, Infection Prevention, and Hawai'i DOH coordinated contact precautions and surveillance; no subsequent spread was detected and the patient fully

Key message: travel history + timely microbiology + WGS transformed a single cUTI into an actiona

This is AMR importation made visible: *a travel exposure became a resistant infection, WGS identified the high-risk clone and resistance genes, and coordinated reporting prevented local transmission.*

Kamau E, et al. Complicated urinary tract infection due to an extensively resistant Escherichia coli in a returning traveler. MSMR. 2023;30(8):6–9.

Three Concrete Asks

1. Close the gap in your own institution/country — push for the ~12% NAP laboratory-financing gap to close where you work

2. Build or join a regional surveillance/data-sharing network — GLASS, Africa CDC AMRSNET, ASLM

3. Treat every unusual isolate as a potential sentinel — report it

Diagnostics are not an afterthought to stewardship, surveillance, and security — they are the precondition for all three

Final Thoughts — Thank You. Questions & Discussion.

A base-pair mutation and a hospital in Djibouti are on the same map.

Diagnostics are not the end of the AMR story — they are the beginning of every other chapter: stewardship, policy, security.

The next resistant, hypervirulent organism is not a future risk — it is already circulating. The only question is whether we can see it.

Edwin.kamau@cepheid.com