Basics of Antimicrobial Stewardship in Hospitals

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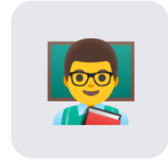

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INTRODUCTION

What is Antimicrobial?

Antimicrobials are agents that either kill microorganisms (biocidal effect) or inhibit their growth (biostatic effect).

While antimicrobials include agents that act against viruses, fungi, and parasites, this presentation focuses on **bacterial infections** and the use of **antibiotics**, which are the most commonly misused and most affected by resistance.

Gram-Positive vs Gram-Negative Bacteria

Bacteria are broadly classified into: **Gram-positive** (e.g. *Staphylococcus aureus*) and **Gram-negative** (e.g. *E. coli, Klebsiella*) based on their cell wall structure.

- **Gram-Positive:** Thick peptidoglycan wall, no outer membrane.
- **Gram-Negative:** Thin wall + outer membrane; often more resistant due to efflux pumps & enzymes.

Major Organisms that Pose Serious Threat to Current Antimicrobial Therapies

Gram-Negative Bacteria

Critical urgent threats

Carbapenem-resistant Enterobacteriaceae (CRE) (e.g. *K. pneumoniae, E. coli*)

Resistant to nearly all beta-lactams, including carbapenems

Pseudomonas aeruginosa

Often resistant to multiple drug classes

ESBL-producing Enterobacteriaceae

Inactivate 3rd-gen cephalosporins

Gram-Positive Bacteria

High Priority

MRSA (Methicillin-resistant *Staphylococcus aureus)*

Resistant to most beta-lactams

VRE (Vancomycin-resistant Enterococci)

Resistant to vancomycin, often multidrug-resistant

Drug-resistant *Streptococcus pneumoniae*

Resistance to penicillin, macrolides

Other Emerging Threats

Neisseria gonorrhoeae

Resistance to fluoroquinolones, cephalosporins, azithromycin

Salmonella (including Typhi)

MDR and extensively drug-resistant (XDR) strains

Mycobacterium tuberculosis (MDR-TB, XDR-TB)

Resistance to rifampicin and isoniazid (MDR); fluoroquinolones and injectable drugs (XDR)

These resistant organisms challenge treatment and highlight the urgent need for **Antimicrobial Stewardship** to preserve antibiotic effectiveness.

What is Antimicrobial Stewardship (AMS)?

Antimicrobial Stewardship (AMS)

Antimicrobial Stewardship is a coordinated program that promotes the appropriate use of antimicrobials, improves patient outcomes, helps reduce antimicrobial resistance, and limits the spread of infections caused by multidrug-resistant organisms.

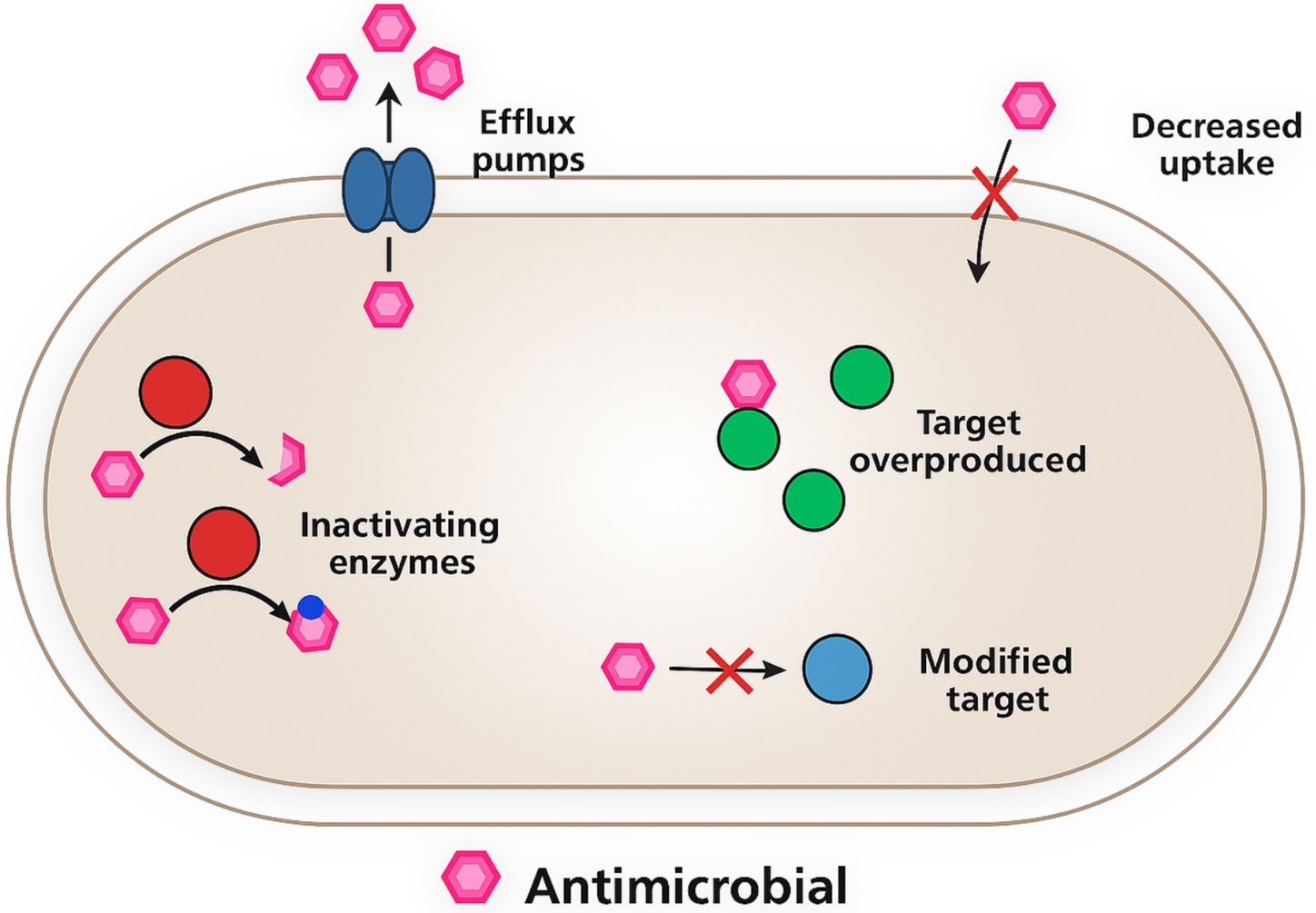
Antimicrobial Resistance (AMR)

- **Antimicrobial Resistance (AMR)** occurs when bacteria, viruses, fungi and parasites no longer respond to antimicrobial medicines (WHO).
- **1.27 million deaths** directly attributed to drug-resistant infections in 2019; **~5 million deaths** associated overall (Murray et al., 2022).
- In **Nigeria alone**, ≈263,000 AMR-related deaths in 2019 surpassing malaria and respiratory infections locally (Murray et al., 2022).

- Resistance mechanism

- **Efflux pumps:** Bacteria actively expel antimicrobials to lower intracellular concentration.
- **Decreased uptake: Reduced** drug entry prevents antimicrobial action.
- **Inactivating enzymes:** Enzymes chemically destroy or modify the drug.
- **Target overproduction:** Excess target dilutes drug effectiveness.
- **Modified target:** Mutation alters the drug's binding site.

Antimicrobial Resistance (AMR) cont’d…



Leading Causes of AMR

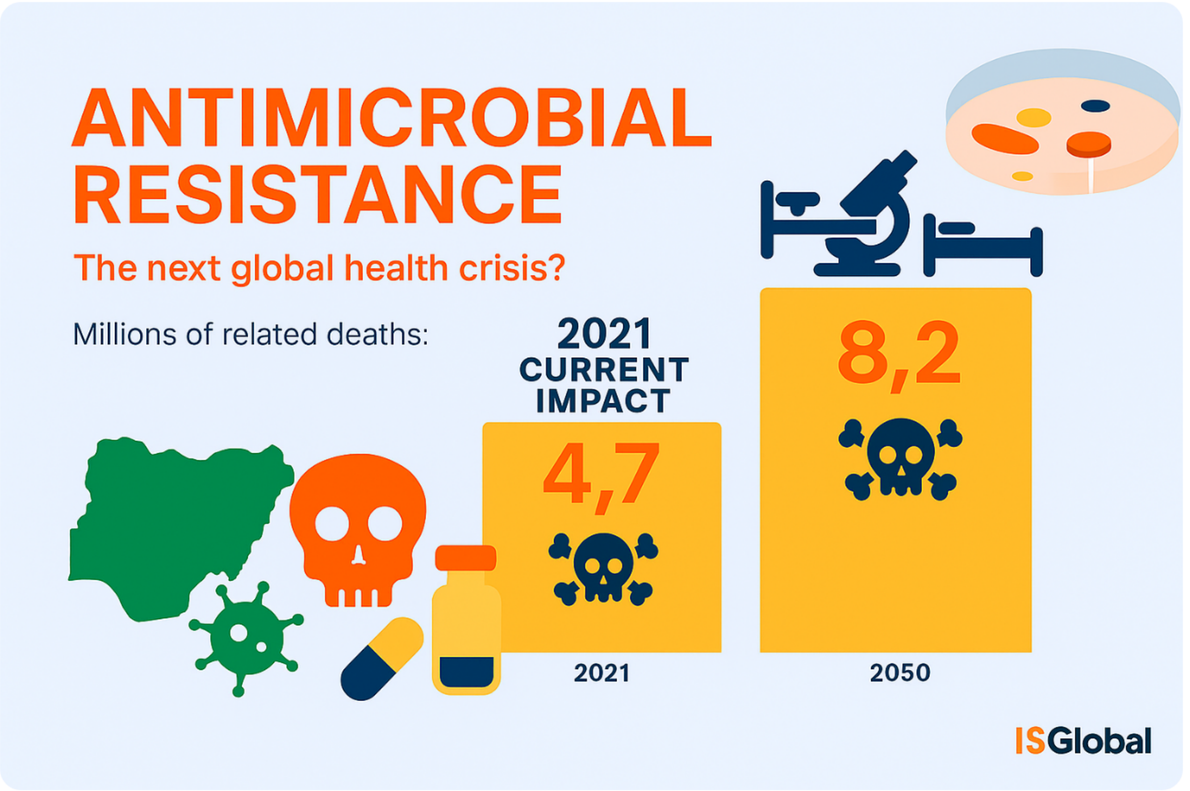
- Overuse & Misuse
- Agricultural Use
- Infection Control
- Innovation Gap

Principles of Antimicrobial Stewardship

- **Appropriate Use of Antimicrobials**
- **Policy and Guideline Development**
- **Multidisciplinary Collaboration**
- **Education and Awareness**
- **Audit and Feedback Mechanisms**
- **Surveillance and Monitoring**

Why AMS Matters in the Hospitals

- **4.7 million deaths** associated with bacterial AMR globally
- **8.2 million deaths** if unaddressed
- **50–70% of hospitalized patients** receive antimicrobials (WHO)
- Increasing local AMR rates leading to **hard-to-treat infections**
- **Resource constraints**: ICU beds, lab diagnostics
- **Economic pressure**: Costs of last-line drugs and extended stays
- Alignment with **Nigeria's AMR National Action**



Historical Evolution of Antimicrobial Stewardship Programs (ASPs)

- 1940s: Sir Alexander Fleming warned about emerging antibiotic resistance
- 1996-97: Term "Antimicrobial Stewardship" was coined by McGowan & Gerding; Incorporated into IDSA guidelines.
- 2007: IDSA/SHEA formally endorse Hospital ASPs as a core strategy.
- 2009 to 13: CDC launched US national stewardship initiatives (Education -> Formal Strategy).
- 2016: WHO & UN General Assembly endorsed global Antimicrobial Stewarship Programs (ASP); WHO issues toolkits.
- Mid-2010s Onwards: Accreditation bodies & governments (e.g., EU 2017) mandate ASPs globally.

Nigerian National Antimicrobial Resistance (AMR) Response

- 2017-22: Launch of 1st National Action Plan (NAP-1.0) on AMR (One Health: Human, Animal, Env.).
- NAP-1.0 Mid-term Review: ~44% activities completed; Gaps identified (e.g., weak environmental/agricultural involvement).
- Oct 2024: Launch of NAP-2.0 (2024-2028) - Aligns with UN/Global Health Security.
- **NAP-2.0 Priorities:**
  - Strengthen ASPs
  - Enhance AMR Surveillance
  - Promote Research
  - Bolster Health Systems (One Health)

ASP Implementation in Nigerian Hospitals so far

- Only 13% to 35% of Nigerian tertiary hospitals have formal ASP teams/committees (Ohaju-Obodo et al., 2020).
- Critical gaps exist: ~24%have local treatment guidelines & only ~12% enforce mandatory antibiotic review/approval.
- Pharmacists commonly perform ad-hoc stewardship (e.g., prescription review) despite lacking formal ASP programs (Ogunnigbo et al., 2021).
- Key barriers: Insufficient AMS/Prof. training, shortage of Prof-specialized pharmacists, & weak administrative support.
- Nigerian hospitals show "significant inadequacies" in ASP implementation.

WHO AWaRe Classification for Antimicrobials/Antibiotics

- WHO groups antibiotics into Access, Watch, and Reserve to guide usage.

Access Group

First-line narrow-spectrum

1. Amoxicillin **(e.g., Amoxil®)**
2. Cotrimoxazole **(Septrin®)**
3. Nitrofurantoin **(Macrodantin®)**
4. Cloxacillin **(Cloxapen®)**
5. Benzylpenicillin **(Crystapen®)**

Watch Group

Higher resistance potential

1. **Co-amoxiclav** **(Augmentin®)**
2. Ciprofloxacin **(Ciprotab®)**
3. Ceftriaxone **(Rocephin®)**
4. Azithromycin **(Zithromax®)**
5. Cefuroxime **(Zinnat®)**

⚠️ Classified as Watch due to ESBL risk

Reserve Group

Last-resort agents

1. Meropenem **(Meronem®)**
2. Colistin **(Colimycin®)**
3. Linezolid **(Zyvox®)**
4. Vancomycin **(Vancox®)**
5. Tigecycline **(Tygacil®)**

🔒 Restricted use (requires consultant approval)

AMS Techniques

Front-End Interventions

Pre-Authorization Strategy

🔒

Approval Required Before Prescribing

Who approves:

- Medical Doctor
- Pharmacist

Pros:

✓ Immediate control of high-risk drugs

✓ Prevents inappropriate use upfront

Cons:

✗ May delay therapy in emergencies

✗ Adds administrative burden

Back-End Interventions

Audit & Feedback Strategy

🔍

Review After Antibiotic Initiation

Who reviews:

- Pharmacist
- Stewardship team

Pros:

✓ Prescriber autonomy preserved

✓ High educational value

Cons:

✗ Labor-intensive

✗ Slower impact (48-72h)

Evidence & Outcomes

- Both strategies are core components of ASPs
- **Hybrid models are common:**
- Pre-auth works well for Reserve drugs
- Audit/feedback is usually practiced on broad-spectrum use
- Studies show reduced resistance and improved prescribing behavior

The “4 Ds” of Antimicrobial Prescribing

💊 1. Right Drug

- Select the most targeted antimicrobial/antibiotic for the infection.
- Avoid broad-spectrum agents unless absolutely necessary.
- Consider local resistance patterns and patient allergies.
- *Example: Use nitrofurantoin for uncomplicated urinary tract infections instead of a fluoroquinolone like ciprofloxacin.*

📏 2. Right Dose

- Tailor the dose to:
- Patient weight
- Renal and hepatic function
- Severity of infection
- Underdosing risks treatment failure; overdosing risks toxicity.
- *Vancomycin dose reduced to once daily in a patient with kidney impairment to prevent toxicity.*

The “4 Ds” of Antimicrobial Prescribing cont’d…

⏳ 3. Right Duration

- Prescribe for the shortest effective course possible.
- Overly long durations increase risk of resistance and side effects.
- Reassess therapy at 48–72 hours and adjust based on clinical response.
- *Example: Community-acquired pneumonia often requires 5–7 days, not 10+.*

🔄 4. De-escalation/Diagnosis

- Once culture and susceptibility results are available:
- Stop unnecessary antibiotics
- Switch from broad-spectrum to narrow-spectrum agents
- De-escalation reduces collateral damage to the microbiome and lowers resistance risk.
- *Example: If vancomycin was started empirically for MRSA, but cultures show MSSA, switch to nafcillin or cefazolinvpvpv.*

The 4 C (Antibiotics) Associated with *Clostridioides difficile* Infection (CDI)

What is *C. difficile?*

Clostridioides difficile Infection (CDI):

A nosocomial infection caused by *C. difficile*, mostly following some antibiotic exposure, resulting in disruption of normal gut flora and colonic inflammation.

- Gram-positive, spore-forming, obligate anaerobe
- Transmitted via fecal-oral route; spores persist on surfaces for prolonged periods
- Risk factors: broad-spectrum antibiotics, hospitalization, advanced age, immunosuppression

THE 4C Antibiotics Associated with CDI Risk

ANTIBIOTIC	RISK LEVEL
1. Clindamycin	HIGH
2. Cephalosporins	HIGH
3. Co-amoxiclav	HIGH
4. Ciprofloxacin	HIGH

SYMPTOMS of *C. DIFFICILE* INFECTION

WATERY DIARRHEA

(≥3 loose stools in 24 hours)

SYSTEMIC SYMPTOMS

- Fever
- Abdominal pain/cramping

SEVERE COMPLICATIONS

- Pseudomembranous colitis
- Toxic megacolon
- Colonic perforation

PHARMACEUTICAL IMPORTANCE OF AMS

PHARMACEUTICAL IMPORTANCE OF ANTIMICROBIAL STEWARDSHIP

💊 Ensures **rational drug use** and prescribing accuracy

🦠 Reduces **antimicrobial resistance** and *C. difficile* infection rates

💰 Promotes **cost-effective therapy** and optimal patient outcomes

🌍 Aligns with **global frameworks** (WHO AWaRe categories)

Pharmacist-Led Stewardship Activities

Pharmacist-Led Stewardship Activities cont'd...

Formulary Development

- Leverage AWaRe categories to decide which antibiotics to stock and restrict
- Use local antibiogram data to guide first-line agents
- Example: Nigerian teaching hospitals built an AWaRe-based formulary in partnership with health authorities

Pharmacist-Led Stewardship Activities cont'd...

Drug Audits (Prospective Audit & Feedback)

- Review each prescription's indication, choice, dose, and duration.
- Provide real-time feedback to prescribers
- Track Days of Therapy (DOT), Defined Daily Doses (DDD), and C. difficile rates
- Conduct routine medication chart reviews or AMS rounds to educate clinicians

Pharmacist-Led Stewardship Activities cont'd...

IV-to-Oral Switch

- Identify patients eligible for transition from IV to oral antimicrobial.
- Studies show pharmacy-led protocols can shorten median IV courses(e.g., from 3 to 2 days), reduce costs, and decrease length of stay
- Frees IV lines and beds while maintaining clinical efficacy

Pharmacist-Led Stewardship Activities cont'd...

Education

- Teach medical and nursing staff AMS principles, AWaRe categories, dosing/duration norms, and infection control
- Utilize in-service trainings, case reviews and ward-round presentations
- CDC core elements emphasize pharmacist-led teaching as a stewardship cornerstone

Pharmacist-Led Stewardship Activities cont'd...

Guideline Implementation

- Lead development and rollout of facility-specific antibiotic guidelines and order sets (e.g., pneumonia, sepsis, UTI)
- Embed protocols into electronic order systems and standard treatment guidelines (STGs)
- Ensure guidelines reflect local antibiogram data and national STGs

Pharmacist-Led Stewardship Activities cont'd…

Leadership

- Serve as AMS champions or co-leads of the stewardship program
- Liaise with Pharmacy & Therapeutics committees to drive policy and formulary changes
- Advocate for stewardship culture and interprofessional collaboration

Conclusion

Antimicrobial Stewardship (AMS) is vital for **safe and effective hospital care.** **Pharmacists** are central to its success, helping improve patient outcomes and combat **resistance.** FMC Keffi has much to gain from AMS, and with strong leadership can become a model for stewardship excellence and example to other hospitals in Nigeria.

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Thanks For Listening!

Questions and Discussions